A T H E S I S

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by

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A STUDY in some PHASES of TUBERCULOSIS, with special reference to the Incidence of BOVINE INFECTION and the Question of LATENCY and PREVALENCE of the DISEASE.

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OBJECT.

The present investigation has been undertaken with the object of obtaining information as to

(a) The relative incidence of the bovine and human types of tubercle bacillus in the infection in man.

(b) The phenomena of latent tuberculous infection in a series of patients dying from causes other than tuberculosis, and in whom no tuberculous lesions could be demonstrated, on naked eye examination, and

(c) The question of prevalence of tuberculosis.

At the same time the morphological and cultural characters of the human and bovine tubercle bacillus were observed, and the portals of entry through which tubercle bacilli may invade the human body have also received attention.

INTRODUCTION/

INTRODUCTION.

The research was begun in October 1913, and was conducted in the Royal College of Physicians' Laboratory, Edinburgh, at the suggestion and under the supervision of Professor James Ritchie. The original material for the investigation was obtained in the majority of cases from the Pathological Department of the Royal Infirmary, Edinburgh; the remaining cases from the Royal Hospital for Sick Children, Edinburgh, and other sources. Care has been taken to avoid, as far as possible, any element of selection, that is, all material obtained from the different sources was examined regardless of the type of infection or presumed mode of origin of such tuberculous lesions as might be present.

The cases are divided, for purpose of description, into four groups.

I. Cases which showed definite lesions of tuberculosis in the body on macroscopic examination; these are sub-divided according to the mode of origin of the disease or to the situation of the lesions.

II./

II. Cases, while showing no evidence of a definite existing tuberculous infection in any parts of the body, but which revealed lesions simulating that of a chronic or healed tuberculosis in the form of calcified or caseo-calcareous nodules. Six other cases not showing these lesions and therefore apparently free of tuberculosis are also included in this group. A further tuberculous case is added for comparison.

III. Cases in which, on careful macroscopic examination, either no changes or only a simple increase in size and perhaps softening of one or more glands could be demonstrated, unassociated with any evidence of tuberculosis.

IV. Sputum cases.

The list includes under:-

GROUP I.*

(a) 15 cases of Pulmonary Tuberculosis.

(b) 4 cases of Abdominal Tuberculosis in Adults
4 cases of Abdominal Tuberculosis in Children.

(c)/

*. The cases are classified according to the rules laid down by PARK & KRUMWIEDE (vide infra)

(c) 5 cases of Tuberculous Meningitis in Adults.
5 cases of Tuberculous Meningitis in Children.

(d) 7 cases of General Tuberculosis in Adults.
5 cases of General Tuberculosis in Children.

(e) 2 cases of Tuberculosis of the Skin.

(f) 2 cases of Tuberculosis of the Genito-urinary tract.

(g) 1 case of Tuberculosis of the Bones and Joints.

(h) 1 case of Tuberculous Cervical Adenitis.

GROUP II.

(a) 27 cases of calcified or caseo-calcareous nodules in Adults.
8 cases of calcified or caseo-calcareous nodules in Children.

(b) 3 Normal cases of Adults.
3 Normal cases of Children.
1 Tuberculous case (for comparison).

GROUP III.

22 cases of Adults.
14 cases of Children.

GROUP IV.

Sputum from 32 cases of Pulmonary Tuberculosis.

RESULT/

RESULT OF THE INVESTIGATION OF THE DIFFERENT GROUPS OF CASES.*

GROUP I.

Section (a) Pulmonary Tuberculosis.

In this section the material obtained post mortem from 13 cases of adults and 2 cases of children in which with the exception of one instance (No. 75), the portal of entry for the tubercle bacilli was most probably in the Respiratory tract, (judging from the post mortem findings), has been investigated. Cultures isolated from 14 cases were all of the human type, while in the remaining case (No. 38) the inoculated guinea-pigs died prematurely and no culture was obtained.

I. Case 19. A man, aged 45, died of cerebral haemorrhage. A large phthisical cavity was found in the right lung with tubercular interstitial pneumonia. One mesenteric gland showed much calcification. No evidence of tuberculosis was discovered elsewhere.

Three/

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* The full post mortem records of the cases discussed are given in Volume II. The method of investigation is dealt with separately. (vide infra)

Three strains of cultures were isolated; one from the calcareous mesenteric gland, one from the cervical gland and the third from the lung. On artificial media the three cultures exhibited identical cultural characters, growing slowly and were of low virulence for the rabbit.

II. Case 20. The patient was a woman, aged 31, who died of peritonitis as the result of an intestinal stricture. Both lungs showed excavation at the apex with more recent extension downwards. In the lower lobes numerous clusters of lymphoid tubercles were seen. Elsewhere there were no tuberculous lesions.

A culture isolated from the bronchial gland produced luxuriant growth and was of low virulence for the rabbit.

III. Case 24. The case was that of a male, aged 31, who died of phthisis and waxy Kidney. A considerable number of old fibrous tubercles in the left upper lobe and scattered miliary tubercles in the lower lobe were found. There were numerous submiliary cavities in the right lower lobe. The peritoneum/

peritoneum was studded with tubercles and so was the omentum and serous coat of the intestines.

Three strains of cultures were obtained - viz. from the bronchial gland, the lung and the diaphragm; they were all eugonic and for the rabbit those from the bronchial gland and diaphragm were of low virulence, while the third strain was not tested.

IV. Case 33. The case was that of a man, aged 59, who died of myocarditis and pleurisy. Numerous yellowish tubercles were seen on the outer surface of the pericardium; the left bronchial glands contained numerous minute point like tubercles, while those of the right side were calcified in some instances. Beyond these lesions and a few old calcified nodules in the left lung, there were no tuberculous changes elsewhere.

Cultures isolated from the pericardium and the bronchial gland were both eugonic and of low virulence for the rabbit.

V./

V. Case 34. The patient was a girl, aged 12, who died of pulmonary tuberculosis. There were numerous small cavities in the right lung and caseous broncho-pneumonia in the left; the small intestine showed many ulcers evidently of recent formation while the other organs were not affected.

A culture isolated from the lung was eugonic and of low virulence for the rabbit.

VI. Case 38. The case was that of a man who died of heart disease. A large phthisical cavity was present in the left lung and the intestines showed numerous typical tuberculous ulcers.

No culture was obtained.

VII. Case 53. The woman of this case, aged 36, died of tuberculous peritonitis. A phthisical cavity was present in each lung and the rest of the organ showed miliary tubercles. The abdominal contents were matted together and covered with purulent material. Several caseating areas in the form of cysts were found in the left kidney.

A culture obtained from the lung was eugonic and of low virulence for the rabbit.

VIII. Case 75. The case was that of a child, aged $1^{5}/_{12}$, who died of tuberculosis. The left lung showed numerous small yellowish caseating patches of consolidation, and two areas of tuberculous broncho-pneumonia were demonstrated in the right; there were numerous subperitoneal tubercles lying in the wall of the small intestine. The glands of the neck were enlarged, one to the size of a large walnut, and caseous; those of the thorax and abdomen also showed enlargement but to a less degree. The primary seat of invasion was probably in the tonsils.

A culture isolated from the mesenteric gland was eugonic and of low virulence for the rabbit.

IX. Case 78. The patient was a woman, aged 24, who died of acute nephritis. Numerous tubercles in both lungs were found with many caseous areas surrounded by fibrous tissue; also numerous transverse ulcers were/

were demonstrated in the small intestine.

A culture isolated from the bronchial gland, grew luxuriantly and for the rabbit was found to be of low virulence.

X. Case 91. The case was that of a woman, aged 49, who died of diabetes mellitus. A large phthisical cavity was found in the left lung with some scattered small tubercles and white patches of tuberculous broncho-pneumonia. There was no evidence of tuberculosis elsewhere.

A culture obtained from the lung was eugonic and of low virulence for the rabbit.

XI. Case 96. A man, aged 22, died of acute tuberculous broncho-pneumonia. A large phthisical cavity of some standing was found in both lungs and, in addition, there were many small grey patches of recent tuberculous broncho-pneumonia throughout the greater part of the organ. Elsewhere no tuberculous lesions could be demonstrated.

A culture isolated from the bronchial/

bronchial gland grew luxuriantly and was of low virulence for the rabbit.

XIII. Case 100. The patient, a man aged 59, died of delirium tremens. In the right lung there was a fibrous area of old tuberculosis with a cavity; a calcified gland was found also at its root. No other lesions were demonstrable.

From the lung a culture was isolated which grew luxuriantly and was of low virulence for the rabbit.

XIII. Case 103. The case was that of a man, aged 72, the cause of whose death was unascertainable. Excepting an old caseous and calcified area of encapsulated tubercles near the apex of the left lung and some patches of broncho-pneumonia, there were no other lesions of importance to be seen in this or the other organs.

A culture obtained from the lung was eugonic and of low virulence for the rabbit.

XIV. Case 105. The patient was a woman of 23 who died of chronic pleurisy. The right pleura was obliterated with old thick adhesions and both its parietal and visceral layers/

layers were studded with yellow tubercles. The abdominal glands also showed some tubercles. On the surface of the liver were many minute tubercles of recent development and in several of the mesenteric glands small caseous tubercles were seen.

A culture isolated from the bronchial glands was eugonic and of low virulence for the rabbit.

XV. Case 122. The case was that of a man, aged 38, who died of Cystitis and general septic infection. An old tuberculous cavity was present in both lungs. There was also in the right lung a very large crop of miliary tubercular nodules distributed over the surface. The intestines showed numerous small ulcers of more or less recent formation.

Cultures isolated from the bronchial and the mesenteric glands were eugonic and found to possess a low virulence for the rabbit.

SECTION/

SECTION (b) ABDOMINAL TUBERCULOSIS.

IN ADULTS.

Four cases of abdominal tuberculosis in the adult, caused by tubercle bacilli which had most probably gained entrance into the body by way of the alimentary tract, have been investigated. In all these 4 cases the portal of entry, according to the findings of pathological changes, was somewhere in the mucous membrane of the intestines. The cultures isolated from two of these cases, namely Nos. 16 and 108, were of the bovine type.

I. Case 16. The patient was a woman, aged 56, who died of tuberculous peritonitis. Innumerable small grey tubercles were seen on the peritoneum under the diaphragm and over the liver. In the pelvis the tubercles were even more numerous and these were also found over the surface of the uterus and its appendages. There were no signs of tuberculosis elsewhere and none of the glands showed any tuberculous changes.

A culture raised from the peritoneum/

peritoneum showed a growth of the bovine type and was found to possess a high virulence for the rabbit.

II. Case 76. This case was that of a man, aged 36, who died of intestinal obstruction. Minute grey tubercles in the intestine were seen; the omentum was drawn up and greatly thickened and infiltrated with tubercles. None of the glands were enlarged.

Two strains of culture were obtained, one from the mesenteric gland, the other from the peritoneum. On artificial media, the two strains exhibited identical cultural characters, being very luxuriant in growth, and were of low virulence for the rabbit.

III. Case 82. The patient, a woman, aged 19, died of tuberculous enteritis and showed several ulcers in the jejunum. These were considerably contracted and extended round the gut. More ulcers were also found in other parts of the intestines, these being on the whole deeper and more ragged in appearance.

Cultures isolated from the mesenteric/

mesenteric and bronchial glands had the cultural characters of the human tubercle bacillus and were slightly virulent for the rabbit.

IV. Case 108. The case was that of a woman, aged 22, who died of peritonitis. Two ulcers, both of which had reached the serous coat and had perforated, were found in the jejunum; there were also numerous ulcers towards the lower end of the ileum and these were in the form of a ring extending round the whole lumen of the bowel. Beyond the enlargement and caseation of some of the mesenteric glands, there were no signs of tuberculosis elsewhere. In spite of this, however, three strains of tubercle bacilli were raised from the lung, the liver and the Spleen. They agreed in their cultural characters, growing like the bovine tubercle bacillus and were all highly virulent for the rabbit.

IN CHILDREN.

Four cases have been investigated; In three of these, the portal of entry, (judging from the post mortem/

mortem findings) was in the mucous membrane of the intestine, but in the remaining one, namely case 94, the evidence in this respect was inconclusive. The tubercle bacilli isolated from three of these four cases were found to be of the bovine type, while in the fourth case the strain was human.

I. Case 64. The patient was a girl, aged 3½, who died of cerebral thrombosis. The small intestine was found matted together by the omentum; several ulcers were present in the ileum and a large one in the caecum; there were also numerous scattered tubercles on the peritoneum. Many of the mesenteric glands were large and caseous and there were some haemorrhages and thrombosis in the brain.

A culture isolated from the mesenteric gland had the cultural characters of the bovine type and was highly virulent for the rabbit.

II. Case 83. This case was that of a boy, aged 12, who died of general tuberculosis. The post mortem examination showed many adhesions between the intestines and the abdominal/

abdominal wall and also between their loops; the transverse mesocolon was studded with numerous small tubercles and, here and there, pockets containing tuberculous pus were formed between the contiguous loops. The glandular enlargement of the mesentery was in a more advanced condition than elsewhere, and there were present in both lungs well marked recent tuberculous pneumonia.

A culture obtained from a mesenteric gland grew like the bovine tubercle bacillus and was highly virulent for the rabbit.

III. Case 86. The child, aged 11 months, died of acute pneumonia. The mesenteric glands were enlarged and caseous, and the coils of the small intestine were inseparably united by adhesions, due to an advanced tuberculosis affecting the whole peritoneum. There was no evidence of tuberculosis elsewhere.

A culture raised from the mesenteric gland had the cultural characters of the bovine type and was of high virulence for/

for the rabbit.

IV. Case 94. The patient was a child, aged 8, the cause of whose death was uncertain. The cervical glands were found to be moderately enlarged and more or less homogeneous in appearance on section; one gland in addition showed one or two minute yellow caseous looking foci. The bronchial glands were also enlarged and three of the mesenteric glands showed calcification. Besides these and several flat nodules and numerous homogeneous areas in the spleen there was nothing of importance to record elsewhere.

Inoculation into guinea-pigs of the mesenteric and bronchial glands failed to produce tuberculosis. A culture, however, isolated from the Spleen was eugonic and of low virulence for the rabbit.

SECTION/

SECTION (C) TUBERCULOUS MENINGITIS.

IN ADULTS.

Five cases of tuberculous meningitis in the adult have been investigated, in four of which the primary seat of the disease, (judged of by the post mortem findings), was most probably in the Respiratory tract; in the remaining one (Case 15) the evidence points strongly to an origin from the intestine. The tubercle bacilli isolated were in all cases of the human type.

I. Case V. The patient was a man, aged 26, who died of tuberculous meningitis and, on post mortem examination, showed a solitary cavity together with small caseous foci and fibroid change at the left apex. There was well marked flattening of the cerebral convolutions and excess of cerebro-spinal fluid, and also several tuberculous ulcers in the intestine with adhesions between some of the abdominal viscerae.

Cultures were raised from the spinal meninges and from the cervical, the bronchial and mesenteric glands. All the four/

four strains though growing slowly in culture, exhibited a low virulence for the rabbit.

II. Case 15. The case was that of a girl, aged 18, who died of tuberculous meningitis. Tubercular nodules were demonstrated in the brain, and the intestines were found adherent to the abdominal parietes; there were also numerous caseous nodules throughout the peritoneum, and the Fallopian tubes in the pelvis were enlarged and contained caseous masses. Besides a few scattered tubercles on the left pleura there was no evidence of the disease in the other organs.

Cultures were raised from the mesenteric gland, the lung and spinal meninges. They grew slowly but all were of low virulence for the rabbit.

III. Case 32. The patient, a woman of 36, died of tuberculosis of the Pons. The brain showed caseous masses in the crura cerebri and medulla, and there were numerous caseous encapsulated tubercles in both lungs surrounded by grey tubercles spreading along/

along the lymphatics.

A culture isolated from the lung had all the cultural characters of the human tubercle bacillus and was of low virulence for the rabbit.

IV. Case 63. The case was that of a woman, aged 25, who died of tuberculous meningitis. Minute grey tubercles were found at the base of the brain and on the surface of both pleurae.

A culture raised from the lung and bronchial gland possessed the cultural characters of the human type of tubercle bacillus and was of low virulence for the rabbit.

V. Case 113. The patient was a girl aged 19, who died of tuberculous meningitis. Many small tubercles were found in the brain, the lungs and the spleen; the bronchial glands were enlarged and caseous.

Cultures isolated from the bronchial gland, the spleen and the meninges had the cultural characters of the human tubercle bacillus and were slightly virulent for the rabbit.

IN/

IN CHILDREN.

Five cases have been investigated, in three of which (Cases I, 8, and 67) the primary seat of the disease, (judged of by the post mortem findings), was in the intestine; in case 50 the tonsils were probably the portal of entry of infection, while in the remaining one, Case 47, the evidence regarding the portal of entry, was inconclusive.

Cultures isolated from three of these cases were found to be of the bovine type, the other two being human.

I. Case I. The patient, a child of 5 years of age, died of tuberculous meningitis. There was generalised tuberculosis, and the oldest lesions of the disease were found in the intestines and in the mesenteric glands.

Cultures isolated from the cervical, the bronchial, and the mesenteric glands, and the spinal meninges agreed in their cultural characters, growing like the bovine tubercle bacillus, and all were found to possess a high virulence for the rabbit.

II. Case 8. The case was that of a girl, aged 10 years, who died of tuberculous meningitis.

The/

The brain showed numerous sticky tubercles on the surface; there was present in both lungs a recent spread of miliary and submiliary grey tubercles and in the Spleen numerous yellow caseous tubercles. The oldest tuberculous lesions were found in the mesenteric glands, which were much enlarged and caseous, and also in the intestines, in which were present numerous small ulcers of some standing.

Cultures raised from the cervical and mesenteric glands, and the spinal meninges were identical in their cultural characters, growing like the bovine tubercle bacillus, and were all highly virulent for the rabbit.

III. Case 47. The patient, a girl of 4 years old, died of tuberculous meningitis. At the post mortem examination typical tuberculous meningitis was seen, and in the lungs were present numerous miliary tubercles. The intestines showed tuberculous infiltration and some ulceration, with the involvement of the mesenteric glands which were all greatly/

greatly enlarged and in some instances also caseous. The Spleen and Kidneys also shared in the infection.

A culture isolated from the mesenteric gland grew like the human tubercle bacillus and was of low virulence for the rabbit.

IV. Case 50. The case was that of a girl, aged 4 years, who died of tuberculous meningitis. There were found in the brain some tuberculous deposits, and in the right lung was a wide area of consolidation which was extensively caseous. The tonsils were large and firm, and enlarged glands could be traced down both sides of the neck.

A growth obtained from the lung had the cultural characters of the human tubercle bacillus and was found to possess a low virulence for the rabbit.

V. Case 67. The patient was a boy of 14 years old. who died of tuberculous meningitis. The brain showed the presence of a few minute tubercles, and there were found in the Spleen and Kidneys some grey tubercles. The intestines/

Intestines showed a few small tubercles in the mucous membrane, while the mesenteric glands were enlarged and in several instances also caseous. There was absence of tuberculous lesions in the other glands and in the lungs.

A culture obtained from the mesenteric gland had the cultural characters of the bovine tubercle bacillus and was highly virulent for the rabbit.

SECTION/

SECTION (d) GENERAL TUBERCULOSIS.

IN ADULTS.

Seven cases of this nature have been investigated. In one case, No. 14, there was strong evidence of the portal of entry being in the intestine; in three, namely cases 89, 109, and 111, the primary seat of the disease was probably in the Respiratory tract; in the remaining three cases, Nos. 84, 110, and 118, the evidence as to the point of entry was inconclusive. Cultures isolated from two of the cases, Nos. 14 and 118, were found to possess the characters of the bovine type, the others showed those of the human type.

I. Case 14. The patient was a woman, aged 56, who died of tuberculous peritonitis. The lungs showed numerous scattered areas of caseous tubercles; the chief lesions, however, of the disease were in the abdominal cavity, numerous adhesions all resulting from peritonitis being found on the serous surface of old tuberculous ulcers. There was no evidence of the disease elsewhere.

A culture isolated from the lung grew like the bovine tubercle bacillus and was/

was highly virulent for the rabbit.

II. Case 84. The case was that of a patient, aged 17, the immediate cause of whose death could not be traced. The right lung showed recent lymphatic spread of tubercles, and numerous minute foci were also found in the liver. There was an area of ulceration in the intestine and some of the retroperitoneal glands were enlarged.

A culture isolated from the lung had the cultural characters of the human type and was of low virulence for the rabbit.

III. Case 89. The patient, a man of 41, died of tuberculous pleurisy. The left pleura was greatly thickened and formed a huge sac; many scattered tuberculous foci of varying sizes were found in both lungs. In the small intestine there was a large number of typical tuberculous ulcers, and evidence of the disease was also demonstrated in the Spleen, Liver and Kidneys.

A culture raised from the lung grew like the human tubercle bacillus and was of low virulence for the rabbit.

IV./

IV. Case 109. This woman, aged 51, died of general tuberculosis. A cavity was present in the left lung which together with the right showed scattered clusters of tubercles. There was also evidence of the disease in the liver, spleen, kidneys and brain.

Three cultures were raised, one from the lung, one from the rib, and one from the meninges; they were identical in their cultural characters, growing like the human tubercle bacillus and were of low virulence for the rabbit.

V. Case 110. The case was that of a woman, aged 59, the direct cause of whose death could not be determined. The lungs were extensively affected with tubercles and lesions of the disease, were also demonstrated in the spleen and kidneys.

A culture raised from the spleen had the cultural characters of the human type and was of slight virulence for the rabbit.

VI. Case 111. The patient was a man, aged 32, who died of chronic tuberculous pleurisy. The right/

right pleura was found to be thickened with a caseous appearance and extending along the interspace of the lobes of the lung were seen scattered tubercles spreading along the lymphatics. The liver, spleen, kidneys and peritoneum also showed evidence of the disease.

Cultures were raised from the bronchial glands and the meninges; the two strains were identical in their cultural characters and both were of low virulence for the rabbit.

VII. Case 118. The case was that of a man, aged 21, who died of tuberculosis of the Kidney. Both lungs showed a chronic cavity in the apex with clusters of small tubercles lower down. The substance of each kidney was destroyed more or less completely, and, in its place, were several cavities filled with caseous matters. There were present in the mesentery several hard and old calcareous glands, the largest of which was of the size of a pea. The retroperitoneal glands were pale and enlarged.

Cultures/

Cultures were obtained from the retroperitoneal gland and the lungs. They agreed in their cultural characters, growing like the bovine tubercle bacillus, and both were found to possess a high virulence for the rabbit.

IN CHILDREN.

Five cases have been investigated, under this heading. In three of these the evidence as to the portal of entry was inconclusive; in one, Case 27. the point of entry was in the Respiratory tract; while in the remaining one, case 98, there was strong evidence of the primary seat of the disease being in the intestines. In three instances, namely cases Nos. 60, 98 and 114, the tubercle bacilli isolated were of the bovine type, in the others the organism was of the human variety.

I. Case 23. The patient, a child of 4 years old, died of general tuberculosis and showed numerous subpleural tubercles scattered fairly uniformly over the surface of both lungs. The cerebral meninges, spleen, kidneys and liver were also involved as also/

also was the peritoneal aspect of the abdominal organs.

Cultures raised from the Tonsil, the bronchial gland, the lung and the spleen were identical in their cultural characters, growing slowly, and found to be slightly virulent, for the rabbit.

II. Case 27. The case was that of a boy, aged 15, who died of general tuberculosis. The lungs showed miliary tubercles with large caseous foci at their apices. Tuberculous lesions were also demonstrated in the spleen, kidneys, and brain.

Cultures were obtained from the cervical, bronchial and mesenteric glands, and the spinal meninges; they grew slowly but all were of low virulence for the rabbit.

III. Case 60. The patient was a girl of 13 years old who died of acute tuberculous bronchopneumonia. The lungs were found to be thickly studded with innumerable tubercles; the liver, spleen, and kidneys were also affected with the disease, showing numerous tubercles in their substance. In addition, several of the mesenteric glands were caseous./

caseous.

Two cultures were raised, one from the lung, the other from the mesenteric gland; they grew like the bovine tubercle bacillus and both were highly virulent for the rabbit.

IV. Case 98. The case was that of a child, aged 2 years and 10 months, who died of general tuberculosis. The lungs showed caseous tubercular nodules and several grey patches of bronchopneumonia. In addition, the left lung also showed numerous small cavities containing caseous like material. In the intestine numerous ulcers were found which were relatively chronic in character; the glands of the mesentery were enlarged and, in a few, areas of caseation were seen. The brain, kidneys and spleen also shared in the involvement of the disease.

Cultures were raised from the mesenteric gland and brain; they grew like the bovine tubercle bacillus and were found to possess a high virulence for the rabbit.

V/

V. Case 114. The patient was a girl aged 10 years, who died of general tuberculosis. The lungs showed a large number of small grey tubercles scattered all over and, in addition, in the right lung there were areas of caseous pneumonia. In the liver and spleen numerous scattered tubercles were found. The bronchial glands were greatly enlarged and caseous, and in the surface of the mesentery miliary tubercles were present.

Cultures obtained from the bronchial and mesenteric glands were identical in their cultural characters, growing like the bovine type, and both were highly virulent for the rabbit.

SECTION/

SECTION (e) TUBERCULOSIS OF THE SKIN.

Two cases of Lupus have been investigated, one in an adult and the other in a young girl; the material furnishing the cultures, which were of the human type, was obtained in both instances from the diseased area by operation.

I. Case 77. The patient, a man of 34, had complained of trouble in the left foot since he was six years old. The condition very slowly became worse and the affected part had been twice scraped. In spite of treatment, the progress of the disease had not been arrested, and towards the end of 1914 there was present over the left big toe a warty growth with a few inflammatory foci in the skin and around it. He was again operated on, and a piece of the scraping submitted to histological examination, was found to be of a tuberculous nature.

A culture obtained from the scraping grew luxuriantly on artificial media and was only slightly virulent for the rabbit.

II. Case 115. The case was that of a girl, aged 16, who presented on examination an ulcer with raised/

raised edges and rather carcinate outline, situated in the front of the right leg. It had begun six years previously and had since then healed up and broken down several times.

A culture raised from the diseased tissue grew luxuriantly and was of low virulence for the rabbit.

SECTION/

SECTION (f) TUBERCULOSIS OF THE GENITO-URINARY TRACT.

This section includes two cases. Owing to circumstances cultures from one only could be studied. This was found to be of low virulence for the rabbit, and therefore belonged to the human type.

I. Case 70. The case was that of a man, aged 28, who died of lobar pneumonia. The left lung showed some consolidation, and there were found in the left kidney several loculi filled with caseous contents. These were also present in the adhesions between that organ and the pancreas.

A culture raised from the enlarged retroperitoneal gland grew luxuriantly &was of low virulence for the rabbit.

II. Case 85. The patient, a man of 41, died of tuberculous pyelonephritis, and showed extensive tuberculous lesions of the kidneys, testis and epidydymus.

No culture was obtained, as the three guinea-pigs inoculated with a piece of the diseased tissue all died prematurely.

SECTION/

SECTION (g) TUBERCULOSIS OF THE BONES AND JOINTS.

One case has been investigated; the material furnishing the culture, which possessed characters of the human type, was obtained by operation.

Case 29. The patient, aged 3 years and six months, had a history of swelling of the left ankle and leg for 12 months. On examination, the ankle joint was found to be considerably swollen and to present a peculiar boggy feeling to the touch. Von Pirquet's reaction was positive and the X rays showed a definite focus of tuberculosis in the bone.

A culture raised from the diseased tissue of the ankle grew luxuriantly and was of low virulence for the rabbit.

SECTION/

SECTION (h) TUBERCULOUS CERVICAL ADENITIS.

One case has been investigated. The culture isolated from the gland removed by operation was of the human type.

Case 22. The case was that of a woman, aged 22, who was operated on for tuberculous cervical adenitis. The clinical history showed that two months previously the patient first noticed a small lump on the right side of the neck; this had gradually increased in size, slowly and painlessly, and on subjective examination was found to have attained the size of a golf-ball.

A culture raised from the gland had the cultural characters of the human tubercle bacillus and was found to possess a low virulence for the rabbit.

GROUP II.

This section deals with those cases in which calcified or caseo-calcareous glands or nodules were found, unaccompanied by any other obvious existing tuberculous infection in the body.

The object of this part of the investigation was to gain information as to the percentage of cases with such lesions, A. which were capable, on the lesions being injected, of producing tuberculosis in the guinea-pigs, (the presence of living tubercle bacilli being thus demonstrated); or, B. in which tubercle bacilli were shown microscopically in the lesions. Such information must be of some importance, on the one hand, with regard to the question as to how many cases of this nature can be justly regarded as tuberculous, and, on the other hand, as to what in reality constitutes a cured lesion of tuberculosis.

For the better elucidation of this subject it is necessary to divide it into two sections.

A. Cases where the determination was based on animal inoculation.

B. Cases where the result was established on a thorough microscopic examination for the presence of tubercle bacilli.

SECTION A.

Under this heading thirty-five cases have been investigated, of which 27 were adults and 8 children.

The material for the investigation was the calcified or caseo-calcareous glands or nodules found on post mortem examination, and these were inoculated into guinea-pigs in the form of an emulsion. The animals were allowed to live for from 5 to 6 weeks and at the end of that time, if they survived, were killed; when tuberculous lesions were found, cultures were raised for the purpose of determining the type of the tubercle bacillus.

Of the 27 cases of adults, 5 furnished material which was capable of transmitting tuberculosis to the guinea-pigs on inoculation. One specimen was investigated for each case and the total specimens consisted of 11 bronchial glands, 9 mesenteric glands, 1 cervical gland and 6 nodules in the lungs, all being either partly or wholly calcareous in nature. None of the mesenteric and cervical glands were found to be tuberculous on inoculation; of the 11 bronchial glands and 6 pulmonary nodules,

3 and 2 respectively were productive of tuberculosis in the inoculated animals, yielding cultures of the human type in three instances, and of the bovine type in one; in the remaining case no culture was obtained.

Of the 8 cases of children, 2 proved to be tuberculous on animal test. In this series bronchial glands were obtained from three cases, and mesenteric glands from five. As already mentioned, in two instances only did the inoculated animals develop tuberculosis. In both cases the injected material was the mesenteric glands and the cultures obtained belonged to the bovine type.

The following is an account of the cases which were found to be tuberculous on animal test.

5 CASES OF ADULTS.

I. Case 28. The patient was a man of 39, who died of a ruptured aneurism. At the post mortem examination, beyond some bronchial glands being partly calcified, there were no lesions related to tuberculosis demonstrated anywhere in the body.

A culture raised from the calcified glands grew like the bovine type and was/

was found to possess a high virulence for the rabbit.

II. Case 48. The case was that of a man, aged 41, who died of chronic heart disease. The bronchial glands of the right lung were enlarged and one of them showed a small calcareous nodule. Elsewhere lesions pertaining to tuberculosis were not found.

A culture isolated from the calcareous bronchial gland grew luxuriantly and was of low virulence for the rabbit.

III. Case 99. The patient was a man of 60 years old, who died as the result of a malignant tumour. The only lesions in the body simulating tuberculosis were some areas of caseation surrounded by fibrous tissue at the apex of the right lung.

Both the guinea-pigs inoculated with the caseous matter developed tuberculosis, but, owing to an accidental contamination, a culture in this case could not be isolated.

IV. Case 119. The case was that of a woman, aged 57, who died of heart disease. There were no lesions in the body of a tuberculous nature, but/

but there was a fibro-calcareous nodule of the size of a pea at the apex of the left lung.

A culture raised from the calcareous nodule grew luxuriantly and was of low virulence for the rabbit.

V. Case 121. The patient, a woman of 35 years old, died of empyema. Excepting a large calcareous gland, the size of a bean, at the root of the lung, there were no other changes in the body of a tuberculous character.

A culture raised from the calcareous gland had the cultural characters of the human tubercle bacillus and was slightly virulent for the rabbit.

2 CASES OF CHILDREN.

I. Case 74. The patient, a child of 2 years and 6 months old, died of bronchopneumonia. At the post mortem examination the lungs showed numerous grey patches of bronchopneumonia, but unassociated with any evidence of tuberculosis. One group of 3 or 4 glands was present/

present in the mesentery which were massed together and quite caseous.

A culture raised from the caseous glands grew like the bovine type and was found to possess a high virulence for the rabbit.

II. Case 81. The case was that of a child, aged 1 year and 7 months, the cause of whose death was not evident. At the post mortem examination, beyond some mesenteric glands being enlarged and caseous, there were no important changes in the organs or glands to record.

A culture raised from the caseous glands had its cultural characters identical with that of the bovine tubercle bacillus and was of high virulence for the rabbit.

A summary of the thirty-five cases in this group is given in the two following tables. The first table shows the cases which were negative, the second the cases positive on inoculation.

TABLE of 28 NEGATIVE CASES.

TABLE I.

NO. of CASE.	AGE.	*CAUSE of DEATH.	SOURCE of MATERIAL for INOCULATION.	NATURE of MATERIAL.
2	38	Delirium tremens	Cervical gland	Chalky foci.
11	10	?	" "	moderately enlarged
			Bronchial "	little old tubercles
			Mesenteric"	slightly enlarged
12	19	Intestinal Ob-	Cervical "	animal died prematurely
		struction	Bronchial "	slightly enlarged
			Mesenteric"	several calcareous
13	58	?	Bronchial "	partly calcified
17	7	Heart Disease	Cervical "	apparently healthy
			Bronchial "	several calcareous
			Mesenteric"	generally enlarged
18	58	Pernicious Anaemia	Cervical "	apparently healthy
			Bronchial "	partly calcified
			Mesenteric"	slightly swollen
21	48	Nephritis	" "	one large calcareous mass
35	35	Injuries to Back	" "	one calcareous
37	48	Heart Disease	" "	several calcareous
40	28	Cerebral Embolism	" "	one calcified
44	48	Cerebral Haemorrhage	" "	one calcareous
45	58	Fractured Skull	Lung	one calcareous nodule
46	45	Heart Disease	Bronchial "	one partly calcified
49	5	Nephritis	Mesenteric"	one large caseous
51	39	Dysentery ?	" "	one calcareous
59	59	Cerebral Haemorrhage	Bronchial "	a few calcareous nodules

* In some cases determined clinically, in others pathologically.

TABLE I. (Contd.)

NO. of CASE.	AGE.	CAUSE of DEATH.	SOURCE of MATERIAL for INOCULATION.	NATURE of MATERIAL
65	Adult	Cerebral abscess	Bronchial gland	A caseous focus.
66	54	Sarcoma	Lung	1 or 2 calcareous nodules
71	12	Heart Disease	Bronchial gland	slightly enlarged one calcareous
			Lung	A small calcareous nodule.
73	77	?	Bronchial gland	Enlarged, some calcareous
80	9&9/12	Heart Disease	Mesenteric "	Many enlarged some calcareous
97	18	Fractured Skull	" "	1 or 2 calcareous.
101	67	Arterio-Sclerosis	Lung	A caseous area
104	14	Heart Disease	Mesenteric Gland	Several enlarged, one calcareous.
106	28	Bronchitis ?	Bronchial "	Old calcified masses.
107	18	Epilepsy	Gland near Pancreas	One caseous
112	21	Cerebral Haemorrhage	Bronchial gland	One calcareous.
120	64	Exophthalmic Goitre	Lung	A fibro-caseous mass.

TABLE of 7 POSITIVE CASES.

TABLE II.

	NO. of CASE.	AGE.	CAUSE of DEATH.	SOURCE of MATERIAL for INOCULATION.	NATURE of MATERIAL.
	(b) 28	39	Aortic Aneurism	Bronchial gland	Slightly enlarged and partly calcified.
	(a) 48	41	Heart Disease	Bronchial "	Enlarged, one calcareous nodule.
	(b) 74	$2\frac{1}{2}$	Broncho-pneumonia	Mesenteric "	Group of 3 or 4 glands caseous.
	(b) 81	1 & 6/12	?	" "	Some enlarged and caseous.
	(c) 99	60	Epithelioma	Lung	Areas of caseation surrounded by fibrous tissue.
	(a) 119	57	Heart Disease	Lung	A fibro-calcareous nodule.
	(a) 121	35	Pleurisy	Bronchial	Enlarged, one calcareous.

a = cultures isolated belonged to the Human type.

b = " " " " " Bovine "

c = " contaminated."

SECTION B.

Under this section 6 consecutive cases have been investigated, of which 3 were adults and 3 children. The cases, though consecutive, were chosen because they exhibited no clinical evidence of tuberculosis and further, on careful post mortem examination, no evidence of tuberculous lesions were found. In each case the bronchial glands were dissected out, emulsified and inoculated intraperitoneally into three guinea-pigs. A careful and minute examination of both lungs was then conducted, thin slices of the organ being cut out and closely scrutinised for the presence of calcareous or fibrous nodules. If any were discovered, they were taken off and prepared for paraffin sections which were cut in series, stained by Ziehl-Neelsen and examined, section by section, for the presence of tubercle bacilli.

In none of the 3 cases of children were any fibrous nodules discovered; in 2 of the 3 adult cases the presence of such nodules was demonstrated, two in each case; in the remaining third case the search proved negative.

Sections/

Sections amounting in all to 1,081 of these four nodules from the two adult cases were stained and examined for tubercle bacilli, but in none could these be demonstrated. As a control, sections of nodules of an undoubted tuberculous nature were similarly prepared and examined; these readily revealed the presence of tubercle bacilli under the microscope.

PROTOCOL OF THE CASES.

I. Case 123. The patient was a woman, aged 62, who died as the result of a malignant tumour pressing on the common bile duct. There was no evidence of tuberculosis in any part of the body.

The bronchial and root glands of the lungs were normal in size but deeply pigmented. They were dissected out, 15 from the left and 12 from the right side, and inoculated into three guinea-pigs. None of the animals developed tuberculosis.

The right lung was slightly congested and oedematous, with some emphysema at the margins; the left lung was on the whole similar. On careful dissection and ex-/

examination a small fibrous nodule, measured about 4 mm. in diameter, was discovered half an inch from the apex of the left lung. It was dark grey in colour and hard to the touch. A similar nodule, of about 5 mm. in diameter, was also demonstrated about an inch from the apex of the right lung.

A microscopic examination of over 645 sections of these two nodules showed a fibrous capsule of some thickness enclosing within it material of a fibrous nature, but failed to disclose the presence of any tubercle bacilli.

II. Case 124. The case was that of a woman, aged 36, who died of a general peritonitis. No sign of tuberculosis was present in the body.

The bronchial and root glands were dissected out, 7 from the right and 8 from the left; all were deeply pigmented but showed no evidence of disease. On inoculation into three guinea-pigs none of the animals developed tuberculosis.

Both lungs were very congested and oedematous; a series of thin slices of the organ/

organ, on careful examination, did not expose any fibrous or calcareous nocules, nor any signs which could be interpreted as evidence of past or present tuberculosis.

III. Case 125. The patient, a man of 49, died as the result of a fractured skull. At the post mortem examination none of the organs revealed evidence of disease.

The bronchial glands, 8 from the right and 12 from the left side, all being deeply pigmented, were dissected out and inoculated into three guinea-pigs; all the animals remained healthy.

Both lungs presented a healthy appearance on gross examination. In thin slices, there were discovered in the left lung two small round nodules, about 6 mm. and 4 mm. in diameter, in the lower lobe near the pleural surface.

A microscopic examination of over 436 sections of these nodules did not disclose the presence of any tubercle bacilli. One of the nodules was found histologically to consist, in the main, of fibrous tissue, the/

the other of a fibrous wall encircling some suspicious looking caseous material.

IV. Case 126. The case was that of a child, aged 5 months, who died of bronchopneumonia.

The bronchial glands were generally somewhat enlarged, the largest ones approaching the size of a small pea. They were dissected out, 8 from the left and 11 from the right side, and inoculated into three guinea-pigs. None of them developed tuberculosis. The right lung showed, here and there, patches of bronchopneumonia about 3 mm. in diameter; these were especially marked towards the lower lobe. Some areas of collapse were seen at the margins, more particularly at the upper lobe. The left lung was on the whole similar, excepting that here the bronchopneumonia was even more evident. An examination of a series of thin slices of the organ failed to expose any nodules.

Sections, amounting to 193, were prepared from a typical patch of bronchopneumonia in this case and examined; beyond changes/

changes of a bronchopneumonic type, they showed no alterations nor was the presence of any tubercle bacilli disclosed.

V. Case 127. The patient was a child, aged 6 weeks, the cause of whose death was not determined. At the post mortem examination there was no trace of tuberculosis in the body.

The bronchial glands, 9 from the right and 10 from the left side, all normal in appearance, were dissected out and inoculated into three guinea-pigs. All of them remained healthy.

The right lung, pink in colour, showed some degree of emphysema at the margin. Three or four patches of congestion, with a certain amount of inflammation of the bronchioles, were discovered near the root. A similar appearance was present in the left lung generally, Minute examination of the organ in thin slices did not reveal further changes.

VI. Case 128. The case was that of a child, aged 1 year and 1 month, who died of bronchopneumonia and in whom at the post mortem examination/

examination no lesions of tuberculosis were demonstrated.

The bronchial glands were slightly enlarged on both sides, but unaccompanied by any trace of disease. Five glands from the left and seven from the right side were inoculated into three guinea-pigs; none of these animals developed tuberculosis.

The lower lobes of both lungs were deeply congested with, here and there, patches of bronchopneumonia. Elsewhere there was only emphysema. Even in thin slices further examination did not show other changes.

VII. Case 129. This case, in which nodules of a definite tuberculous nature were demonstrated, was taken as a control, as referred to above.

GROUP III.

This part of the enquiry was undertaken with a view to determine (1) the existence and (2) the frequency of latent tuberculous infection in adults and in children. With this object in view, my investigation has been directed to cases which presented on careful examination by the naked eye; no evidence of tuberculous lesions, anywhere in the body.

The cases amount in all to 36, of which 22 were adults and 14 were children. The glands, cervical, bronchial mesenteric or retroperitoneal, which were normal in appearance or in a state of simple lymphoid hyperplasia were carefully removed from the body. Their surfaces were then seared and the glands made into an emulsion for inoculation into guinea-pigs for the purpose of determining the presence or absence of tubercle bacilli. The animals so inoculated were allowed to live for from 5 to 6 weeks and, if at the end of this time found to be tuberculous on post mortem examination, cultures were taken with the object of determining the type of tubercle bacilli present.

Of the 22 cases in adults and of 14 cases

in/

in children, 3 and 1 respectively afforded material capable of causing tuberculous infection in the guinea-pigs on inoculation.

The following is a summarised account of the four positive cases.

I. Case 25. The patient was a man aged 56, who died of heart disease. At the post mortem examination none of the organs were affected with tuberculosis. The cervical and mesenteric glands were slightly enlarged, while the bronchial glands presented a normal appearance. The guinea-pig inoculated with the cervical gland developed tuberculosis; those with the bronchial and mesenteric glands remained healthy.

A culture isolated from the cervical gland, which histologically showed some congestion, grew like the human tubercle bacillus and was of low virulence for the rabbit.

II. Case 52. The case was that of a woman, aged 61, who died of a terminal pneumonia following lupus erythematosis. At the post mortem examination no trace of tuberculous lesions in/

in the body could be discovered. None of the glands showed any signs of disease, except some along the Aorta and pancreas which were swollen and congested. A section of the gland showed on microscopic examination diffuse fibrosis and pigmentation.

A culture raised from the glands mentioned grew luxuriantly and was of low virulence for the rabbit.

III. Case 54. The patient, a boy 3 years and 6 months old, died of acute osteomyelitis of the Tibia. Numerous abscesses of the lungs were found on post mortem examination and the other organs showed extreme cloudy swelling. Other than enlargement and congestion of some of the mesenteric glands, there were no changes in the glands. A microscopic examination of a section of the mesenteric gland failed to reveal any sign of tuberculosis.

The culture isolated from the mesenteric glands grew like the human tubercle bacillus and was slightly virulent for the rabbit.

IV./

IV. Case 72. The patient was a woman of 28, who died as the result of softening of the brain. At the autopsy the lungs showed congestion and oedema, and there was present at the hepatic flexure of the intestine an area of ulceration with fibrous changes in the thickened wall. Some of the retroperitoneal glands and glands in the gastric-hepatic omentum were greatly enlarged but presented no naked eye evidence of tuberculosis. A microscopic examination of a section of the gland. showed, however, areas of caseation and fibrosis.

A culture isolated had the cultural characters of the bovine type and was highly virulent for the rabbit.

A Summary of the 36 cases into a tuberculous and a non-tuberculous group gives the following two tables.(III. & IV.)

TABLE III. 32 cases showing no evidence of tuberculosis on microscopic examination and on animal inoculation.

TABLE III.

NO. of CASE.	AGE.	CAUSE of DEATH	SOURCE of MATERIAL for INOCULATION.	NATURE of MATERIAL.
3	43	Injuries to Spine	Cervical gland	Slightly enlarged
			Bronchial "	Enlarged, pigmented
			Mesenteric "	Apparently healthy
4	39	Lobar Pneumonia	Cervical "	Slightly enlarged
			bronchial "	" "
			Mesenteric "	Normal
6	36	Myocarditis	Cervical "	Normal
			Bronchial "	Enlarged, pigmented
			Mesenteric "	Slightly enlarged
7	22	Eclampsia	Cervical "	Normal
			Bronchial "	Slightly enlarged
			Mesenteric "	" "
9	64	Heart Disease	Cervical "	Normal
			Mesenteric "	"
			Bronchial "	Animal died prematurely
10	44	Burns	Cervical "	" " "
			Bronchial "	Enlarged, congested
			Mesenteric "	Normal
26	44	Bronchitis	Cervical "	Enlarged, pigmented
			Bronchial "	" "
30	10	Splenic Anaemia	Cervical "	Enlarged
			Bronchial "	"
			Mesenteric "	Greatly enlarged
31	16	Heart Disease	Bifurcation"	Enlarged, oedematous
36	13	Meningitis Pericarditis	Cervical "	Greatly enlarged
			Mesenteric "	Moderatly "

TABLE III. (Contd.).

NO. of CASE.	AGE.	CAUSE of DEATH.	SOURCE of MATERIAL for INOCULATION.	NATURE of MATERIAL.
39	35	Heart Disease	Cervical gland	Animal died prematurely
			Bronchial "	" " "
41	19	Heart Disease	Mesenteric "	Slightly enlarged
42	28	Intestinal Obstruction	Mesenteric "	Moderately "
43	11	Cerebral Apoplexy	Mesenteric "	Enlarged
55	29	Peritonitis	Mesenteric "	Enlarged, several
56	22	Diabetes	Mesenteric "	A chain enlarged
57	45	Malignant Disease	Mesenteric "	Generally "
58	10	Broncho-pneumonia	Cervical "	Enlarged
			Mesenteric "	"
61	12	?	Mesenteric "	Generally enlarged
62	13	Osteomyelitis	Mesenteric "	" "
68	3	Pneumonia	Mesenteric "	Some "
69	7½	?	Mesenteric "	"
79	52	Lymphadenoma	Cervical "	Greatly "
87	3	Broncho-pneumonia	Mesenteric "	"
88	3¾	" "	Mesenteric "	A dozen "
90	1½	Intussusception	Mesenteric "	Throughout "
92	7	?	Cervical "	Markedly "
			Mesenteric "	Enlarged & massed together
93	20	Syphilis ?	Cervical "	" " pale
			Mesenteric "	" " "
95	37	Malignant Disease	Mesenteric "	A great mass of enlarged glands
102	38	Heart Disease	Bronchial "	Enlarged

TABLE III. (Contd.)

No. of CASE.	AGE.	CAUSE of DEATH.	SOURCE of MATERIAL for INOCULATION.	NATURE of MATERIAL.
116	47	Heart Disease	Mesenteric gland	A round cystic body
			Spleen	Grey tubercles?
117	24	Heart Disease	Bronchial and Mediastinal gland	Enlarged, congested

TABLE IV.

Three cases showing neither macroscopic nor microscopic evidence of tuberculosis but proving to be tuberculous on animal inoculation.

No. of CASE.	AGE.	CAUSE of DEATH.	SOURCE of MATERIAL for INOCULATION.	NATURE of MATERIAL.
(a) 25	56	Pericarditis, Nephritis.	Cervical gland	Slightly enlarged
(a) 52	61	Heart Disease. Lupus Erythematosis	Glands near pancreas	Swollen, congested
(a) 54	$3\frac{1}{2}$	Osteomyelitis	Mesenteric gland	Soft, congested
(b) 72	28	?	Retroperitoneal Gland	Greatly enlarged

(a). Cultures isolated belonged to the Human type.
(b). Microscopic examination of a section of the gland showed definite tuberculous changes, therefore it cannot be strictly considered as a case of latent tuberculosis. A culture isolated was of the Bovine type.

GROUP IV.

SPUTUM.

The object of this enquiry was to determine the type of tubercle bacilli isolated from the Sputum which was brought to the Laboratory for examination and in which tubercle bacilli were found.

The Sputum from 32 persons was studied and in 29 of the cases cultures were isolated and tested as to their virulence; in the remaining three cases no investigation could be made, as in two instances the cultures obtained were subsequently found dead in spite of repeated sub-cultures and in the third case both guinea-pigs inoculated for the isolation of the tubercle bacilli died prematurely.

METHOD OF OBTAINING CULTURES.

Two methods have been adopted in obtaining primary cultures, "Indirect" and "Direct".

"Indirect Method" (by animal inoculation). The sputum was inoculated intraperitoneally into two or/

or more guinea-pigs in each case, and cultures were obtained from those which did not die prematurely. If very thick in consistency, it was previously diluted with saline solution before being inoculated. By this method 15 cultures were isolated and studied.

"Direct Method". Cultures were isolated in 14 instances. The sputum, in the condition when brought to the Laboratory, was put into a sterile bottle and, depending on its thickness, such amount of saline solution was added that the resulting mixture was of a thin mucoid consistence. To this Antiformin of such an amount was added that it would constitute in the whole mixture a percentage of between 20 and 25. The diluted sputum was then stirred up, and after being put aside for an hour at a temperature of 37°C. was centrifuged. (This time at this temperature was found sufficient for the sputum to dissolve and for the extraneous organisms necessarily associated with the tubercle bacilli in such cases to be killed off). The deposit was washed with saline solution, recentrifuged, and after this process had been repeated twice, was then sown on egg medium as prepared by DORSET (1).

My experience based on the results obtained by the use of Antiformin in the isola-

tion/

isolation of tubercle bacilli, in so far as sputum is concerned, fully confirms the extreme usefulness of this procedure over that by animal inoculation, in that time and expense is saved and that the chances of obtaining a pure culture are nearly, if not, equally as great. With this Antiformin method I was able to obtain primary cultures in 14 instances out of 18 specimens of sputum. The RoyAL COMMISSION (2) in their investigation have, in part, employed this method with success in obtaining primary cultures from material other than sputum.

BROWN and SMITH. (3) were successful in raising cultures by the use of Antiforim from 33 out of 35 sputum cases.

Similar result was also obtained by PATERSON (4) who recommends a strength of 20% Antiformin in the whole solution, that is, 10.cc. of sputum plus 2·5 cc. Antiformin left at room temperature for 24 hours or for from 4 to 6 hours at 37°C. He did not find any apparent interference with the viability of the bacilli, as the growth occurred at the same rate as in the case of those not so treated.

CRUICKSHANK/

CRUICKSHANK (5) amongst others found it not only useful for isolating cultures direct from sputum but also for the detection of tubercle bacilli in sputum which has yielded negative result with the ordinary smear preparation. He advocates the use of a strength of from 15 to 20% Antiformin in the whole mixture.

Working with a large number of cases, GRIFFITH (6) has extensively employed this method of isolation of tubercle cultures from sputum and found it quite reliable and serviceable. He, however, noticed a distinct inhibitive action on the vitality of the tubercle bacilli, should the Antiformin be left beyond a certain length of time.

Antiformin as originally prepared by UHLENHUTH and XYLANDER (7) consistsd of 7·5% of Sodium Hydrate and such amount of Sodium Hypochlorite that 100 grammes of the mixture liberated 5·3 grammes of Chlorine gas. For ordinary purposes equal parts of Liquor Sodium Chlorinata of the British Pharmacopoea and Sodium Hydrate (15%) answers very well.

STRAINS/

STRAINS ISOLATED.

All the strains isolated, 29 in number, were tested on rabbits as to their virulence and their cultural characters were also observed. On these two tests alone the cultures were classified as "Human" or "Bovine". The procedure in a case, once a primary culture was isolated, was precisely the same as that described elsewhere in this work(vide infra). Briefly, in all instances the cultural characters were noted and, in addition, 0·01 mgm. of the dried tubercle bacilli was inoculated intravenously into the rabbit, and the resultant pathological changes noted.

Twenty-eight of the twenty-nine strains isolated produced in rabbits either a retrogressive or slowly progressive tuberculosis, similar to that caused by bacilli of the Human type. The remaining culture, designated S3, showed well marked cultural characters of the Bovine type and was of high virulence for the rabbit. A rabbit inoculated with 0·01 mgm. of this culture died on the 35th day after inoculation and, on post mortem examination, showed extensive tuberculosis of a rapidly progressive type.

The/

The lungs were voluminous and literally studded all over with small tubercles. The spleen was greatly enlarged and showed innumerable minute tubercles on the surface. The liver was likewise affected, and so were the kidneys, though to a less extent. The virulence of this strain was again tested, and the inoculated rabbit, dead on the 29th day after inoculation, also presented on examination extensive tuberculous lesions of the same rapidly progressive character.

The pathological lesions in this case therefore conformed in every way to that produced by the tubercle bacilli of the bovine type, and the cultural and inoculation tests thus established the complete identity of this culture with that of bovine tubercle bacilli.

The appended table shows the results obtained by various investigators up to the present moment on the subject of the types of tubercle bacilli found in sputum. It is worthy of note that of the 962 cases recorded cultures from 3 were found to be a mixture of human and bovine tubercle bacilli, while from 4 . a pure culture of the bovine type was isolated. Of these latter cases, all occurred in this country, Edinburgh contributing two.

TABLE V.

AUTHORS	TOTAL	HUMAN	BOVINE	MIXED
(8) Various Authors	158	156		2(a)
(9) Lindemann	41	40		1
(10) Weber & Dieterlen	9	9		
(11) Dieterlen	50	50		
(12) Vagedes	6	6		
(13) Kitasato	152	152		
(14) Smith	6	6		
(15) Link	1	1		
(16) Fibigen & Jensen	20	20		
(17) Park & Krumwiede	291	291		
(18) Royal Commiss.1911	28	26	2	
(19) Bulloch	23	23		
(6) Griffith (London)	105	105		
" (Edin.)	43	42	1	
Own cases (Edin)	29	28	1	
	962	955	4	3

(a) cases of De Jong Stuurman and Kossel

The following is an account of the seven cases from which bacilli of the bovine or mixed human and bovine type were isolated.

The de Jong-Stuurman's case (6).

"The patient was a peasant woman, aged 27. A glycerine serum culture from the sputum produced fatal general tuberculosis in three calves. - - - - - No rabbits were tested. The culture is stated to have grown luxuriantly. Only one sample of sputum was investigated". . . . . .

KOSSEL'S CASE (6).

"The patient was a female letter carrier, aged 27 years. Sputum for investigation was collected twice - once on May 30th, 1910, and again on June 4th, 1910. From the first sample of sputum a culture of human type was isolated through the guinea-pig and a culture of bovine type was obtained through the rabbit. From the second sample of sputum, a pure culture of human tubercle bacilli was isolated direct: a mixed culture was obtained from a guinea-pig which had been inoculated with the sputum, and a bovine culture was isolated from a rabbit which had been inoculated with a particle of the spleen of the guinea pig".

LINDEMANN'S/

LINDEMANN'S CASE (6).

"The patient was a musician, male, aged 20 years. Three samples of sputum were investigated. A culture isolated from each sample through the guinea-pig grew on broth like the human tubercle bacillus. - - - - The rabbit culture obtained was dysgonic and highly virulent for calves and rabbits, A virulent culture was also derived from a guinea-pig which had been inoculated with the second sputum sample". - - - -

BRITISH ROYAL COMMISSION'S CASES (18).

I. The patient, aged 21 years, was a butcher by occupation. He has had pneumonia and pleurisy ten months before admission, and had suffered from cough since then. The clinical signs showed consolidation of the upper part of the lower lobe of the left lung. Cultures from the first sample of sputum, isolated through the guinea-pigs, were identical in cultural characters and virulence for the calf, rabbit, and guinea-pig, with the bovine tubercle bacillus. Three other samples of sputum were collected at intervals of 76, 117, and 118 days respectively after the first. All the strains agreed with/

with those first isolated in their cultural characters and proved highly virulent for rabbits.

2. The patient was a man aged 31 years, a bricklayer by occupation. He had pneumonia on the left side when 20 years old, and pleurisy four months before admission. A culture isolated from the sputum through guinea-pigs exhibited the cultural characters of the bovine type and was highly virulent for calves, rabbits and guinea-pigs; the second specimen of sputum collected 118 days after the first, yielded cultures identical in cultural characters and virulence for the calf and rabbit with the culture first obtained.

GRIFFITH'S CASE (6).

The patient was a girl aged 16 years and 7 months, a die stamper by occupation. She was a breast-fed child and had had no serious illness previously. She was in the habit of drinking unboiled milk until shortly before admission to the hospital. There was dulness at both apices, and slight dulness over the right lower lobe. Three specimens of sputum were collected at intervals of three weeks each, and were found to possess cultural characters and virulence for rabbits, identical with those exhibited/

exhibited by the bovine tubercle bacillus.

OWN CASE.*

The patient was a man of 41 years old who had had a somewhat severe attack of haemoptysis two years previously and, preceding this, also two attacks of pleurisy. He recovered sufficiently to take things very quietly, although still unable to attend to work. In spite of Sanatorium treatment and careful feeding, the disease, affecting both lungs, appeared to make slow, steady progress. Dyspnoea was a prominent symptom during the latter half of his illness, and became ultimately so marked that the slightest exertion was liable to bring it on. He died suddenly, as the result of a self-inflicted wound on the neck.

The seven persons referred to above, in whose sputum bovine tubercle bacilli was isolated, either in a pure or mixed strain, all died, but, unfortunately, no post mortem examination was made in any of them.

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* For the clinical notes of this case I am indebted to Dr.Edward M.Tyrell of Galashiels.

TABLE VI.

TABULAR SUMMARY of the RESULTS of the INVESTIGATION of 88 cases from which cultures were isolated and studied out of a total of 129 Hospital cases & of 29 Sputum cases.

GROUP I. SECTION (a) PULMONARY TUBERCULOSIS.

NO. of CASE.	AGE.	SOURCE of CULTURE. 15 Cases.	RESULT
19	45	Cervical gland	Human
		mesenteric "	"
		lung	"
20	31	bronchial "	"
		lung	"
24	31	bronchial "	"
		~~lung~~ diaphragm	"
33	59	bronchial "	"
		pericardium "	"
34	12	lung	"
* 38	58	No culture obtained	---
53	36	lung	Human
75	1 & 5/12	mesenteric gland	"
78	24	bronchial "	"
91	49	lung	"
96	22	bronchial "	"
		~~mesenteric "~~	"
		lung	"
		~~spine "~~	"
100	59	lung	"
103	72	"	"
105	23	bronchial "	"
122	38	" "	"
		mesenteric "	"

*Case found to be tuberculous but cultures not obtained.

SECTION (b) ABDOMINAL TUBERCULOSIS.

NO. of CASE.	AGE.	SOURCE of CULTURE. (8 CASES)	RESULT.
16	56	peritoneum	Bovine
64	3½	mesenteric	"
76	36	peritoneum	Human
		mesenteric gland	"
82	19	bronchial gland	"
83	12	mesenteric gland	Bovine
86	11/12	mesenteric gland	"
94	8	Spleen	Human
108	22	lung	Bovine
		Spleen	"
		liver	"

SECTION (c) TUBERCULOUS MENINGITIS. (10 Cases)

1	5	mesenteric gland	Bovine
		bronchial "	"
		cervical "	"
		meninges	"
5	26	cervical gland	Human
		bronchial "	"
		mesenteric "	"
		meninges	"
8	10	cervical gland	Bovine
		mesenteric gland	"
		meninges	"
15	18	mesenteric gland	Human
		lung	"
		meninges	"
32	36	lung	"
47	4	mesenteric gland	"
50	4	lung	"
63	25	bronchial gland and lung	"
67	14	mesenteric gland	Bovine
113	19	bronchial gland	Human
		Spleen	"
		meninges	"

SECTION (d) GENERAL TUBERCULOSIS. (12 Cases)

14	56	lung	Bovine
23	4	tonsil	Human
		bronchial gland	"
		lung	"
		Spleen	"

SECTION (d) GENERAL TUBERCULOSIS. (Contd.)

NO.of CASE	AGE.	SOURCE of CULTURE	RESULT.
27	15	cervical gland	Human
		bronchial "	"
		mesenteric "	"
		meninges	"
60	13	lung	Bovine
		mesenteric gland	"
84	17	lung	Human
89	41	lung & pleura	"
98	2 & 10/12	mesenteric gland	Bovine
		brain	"
109	51	lung	Human
		rib	"
		brain	"
110	59	Spleen	"
111	32	bronchial gland	"
		Spleen	"
114	14	bronchial gland	Bovine
		mesenteric gland	"
118	21	lung	"
		retroperitoneal gland	"
	SECTION (e)	TUBERCULOSIS of the SKIN. (2 Cases)	
77	34	Tissue from Ankle	Human
115	16	Tissue from leg	"
	SECTION (f)	TUBERCULOSIS of the GENITO-URINARY TRACT. (2 Cases)	
70	28	glands along Aorta	Human
*85	41	No culture obtained	-

SECTION (g) TUBERCULOSIS of the BONES & JOINTS.

(1 Case)

NO.of CASE	AGE.	SOURCE of CULTURE.	RESULT.
29	3½	Tissue from Ankle	Human

SECTION (h) TUBERCULOUS CERVICAL ADENITIS
(1 Case)

22	22	cervical gland	Human

GROUP II	SECTION (a)	CALCIFIED or CASEO-CALCAREOUS NODULE. (35 Cases)	
28	39	bronchial gland	Bovine
48	41	bronchial gland	Human
74	2½	mesenteric gland	Bovine
81	1½	mesenteric gland	"
99	60	lung	No culture obtained
119	57	lung	Human
121	35	bronchial gland	"

The 28 remaining cases were free from tuberculosis.

SECTION (b).

6 Normal Cases and 1 Further Case for Comparison

GROUP III. NORMAL or ENLARGED GLANDS.
(36 Cases)

NO.of CASE.	AGE.	SOURCE of CULTURE.	RESULT.
25	56	cervical gland	Human
52	61	glands near pancreas	"
54	3½	mesenteric gland	"
72	28	retroperitoneal gland	Bovine

The 32 remaining cases were free from tuberculosis.

GROUP IV. SPUTUM.

1 case = Bovine
28 cases = Human

In the 3 remaining cases, no cultures were obtained.

HISTORICAL SKETCH.

Description of the disease, Tuberculosis, in its clinical aspects, dates from Hippocrates, but it was not until the 17th century that accurate observation was made by F.SYLVIUS (1614-1672), who first indicated the connection between tuberculous nodules and phthisis. REID (1785) and MATTHEW BAILLIE (1793) laid the foundation of our knowledge of the close relationship between tuberculosis and consumption in their gross characteristics, but our first definite insight into the nature of the disease occurs in a contribution by BAYLE in the 19th century (1774-1816) on the structure of the tubercle and on its identity in the widely distributed lesions, and later by LAENNEC (1) in 1819, who first recognised the unity of the forms of tubercle - the miliary granule, the infiltration and the caseous mass.

VILLEMIN (2) placed the infective nature of the disease on a solid experimental basis and in 1868 showed that rabbits inoculated with material of human origin were not so rapidly infected as when the inoculated substance was derived from tuberculous cattle./

cattle.

This was soon confirmed by GERLACH (3) who also demonstrated that calves can be infected by being fed on tuberculous meat. KLEBS (4) in the same year showed the possibility of infection of cattle by human tuberculosis.

VIRCHOW (5) in 1880 emphasized the gross anatomical difference between the different processes of the necrotic changes in bovine and human tuberculosis. Then came the demonstration by KOCH (6) in 1882 of the bacillus of tuberculosis which seemed to establish the identity of tuberculosis in man and in cattle.

It was, however, THEOBALD SMITH (7) who first pointed out in 1898, as the result of many carefully conducted experiments, that the bacilli derived from the tuberculous tissue of cattle differed in fundamental particulars from those obtained from cases of human pulmonary tuberculosis.

KOCH (8) startled the scientific world when he made the important announcement in 1901, that human and bovine tuberculosis are distinct, and that it is almost impossible to produce a general tuberculous infection in cattle by inoculating them with human/

human tubercle bacilli from sputum. He dwelt in his lecture on the relationship between human and bovine tuberculosis and some of the statements made by him at that time may be here quoted.

"Though the important question whether man is susceptible to bovine tuberculosis at all is not yet absolutely decided, and will not admit of absolute decision to-day or to-morrow, one is, nevertheless, already at liberty to say that, if such a susceptibility really exists, the infection of human beings is but a very rare occurrence". *

"I should estimate the extent of the infection by the milk and flesh of tuberculous cattle, and the butter made of their milk, as hardly greater than that of hereditary transmission, and I, therefore, do not deem it advisable to take any measures against it".

The prominence of the man and the startling character of his conclusions, which were practically a reversal of his original views, aroused great interest in the subject, and they have been the means of inciting numerous investigations both in this country and elsewhere. Much valuable and important work, all/

all having a bearing on the relation of human and bovine tuberculosis, has since been done on the continent, in America and in Great Britain; in the latter country, useful experiments have been conducted by Delépine and his pupils in Manchester, by Fraser and Mitchell under the direction of Ritchie in Edinburgh, and by the Royal Commission appointed in August 1901 which, after ten years of arduous labour, have issued in 1911 their Final Reports. The results obtained by the various workers have settled many of the disputed points and in many respects are in direct contradiction to the conclusions arrived at by Koch.

METHOD/

METHOD of INVESTIGATION.

PREPARATION of MATERIAL for INOCULATION.

The methods for raising primary cultures from tuberculous sputum have been already dealt with (vide supra), and there is no need to refer to them further here. As regards the other tuberculous tissue investigated, cultures by the "direct" method were not attempted.

The portions of the tissues for investigation, generally the glands and also such lesions in the other parts of the body as presented special interest, were removed from the body and as these, with the exception of the material obtained by operation, were necessarily contaminated to a more or less extent in the process of conducting the post mortem examination, their surfaces were carefully seared. The material from different sites, after such preliminary treatment, was then separately emulsified in the following way: - it was cut up into minute pieces with scissors and ground to pulp with a pestle in a porcelain mortar: normal physiological saline was then gradullly added, while the grinding was continuously kept up until as fine an emulsion as/

as possible was formed. It was filtered through muslin to strain off the coarse particles, (so that the material could pass through a syringe needle) the filtrate so obtained being then inoculated into the animals. If there was evidence that the material had been grossly infected secondarily by pyogenic organisms, the filtrate before injection was subjected to a treatment with Antiformin (20% in final mixture for ¼ hour at 37°C.) It was afterwards centrifuged and the sediment, after the supernatant fluid had been carefully pipetted off, was suspended in normal saline and then employed for inoculation.

MODE of INOCULATION.

Guinea-pigs were in every instance utilised for the isolation of tubercle bacilli and the intra-peritoneal method of injection was, with few exceptions, the one adopted.

METHOD of RAISING CULTURES.

The animals, if not dead prematurely, were killed at the 5th or 6th week after inoculation and if/

if found to be tuberculous, cultures were raised from the diseased tissue.

PARK and KRUMWIEDE (1) and FRASER (2) prefer the lymph nodes as the source of primary cultures, but in my experience equally good results can be achieved by employing the tubercles in the spleen. The tuberculous tissue was removed, squeezed between the ends of the forceps and then rubbed on the surface of the medium with a spatula. The media used were those of DORSET (3) (plain) and LEBENAU (4) (glycerine egg). These were slightly coloured with alcholic basic fuchsin to facilitate the detection of early primary growth, a method advocated by CRUICKSHANK (5).

The advantage of using egg medium for raising cultures has been shown by, among others, the ROYAL COMMISSION (6) and PARK AND KRUMWIEDE (1).

The tubes were then plugged and sealed with paraffin to conserve the moisture as well as to exclude moulds. The cultures were then examined week by week to watch the progress of growth.

PREPARATION of EMULSION.

A culture on plain egg medium of from 3 to 5 weeks old is employed in every case. In order to/

to obtain good growth at this age, subcultures have to be made frequently. The growth is scraped off with a spatula on to a watch glass of known weight, care being taken to avoid the removal of any of the medium and, as a preliminary, is dried over concentrated sulphuric acid for a few hours. It is afterwards weighed on a delicate balance. An emulsion is then made and, where an intravenous injection into rabbits is to be carried out, diluted to the extent that one cc. = 0·01 mgm. of the dry tubercle bacilli. To get a fine emulsion it is necessary to start with a very small amount of normal saline, the drop adherent to the end of glass rod being the right amount of fluid to use for the purpose. The bacilli can conveniently be emulsified by means of the rod in the watch glass which has been used for weighing and saline solution, gradually added. When a fine suspension has been obtained it is transferred to a conical glass and there the proper dilution is made out.

The/

THE RABBIT TEST for the TYPE OF TUBERCLE BACILLI.

VILLEMIN (9) first noticed the difference of susceptibility of rabbits to the infection of human and bovine tuberculous material, but our real knowledge of this comes from SMITH (10) who in 1896 published his first experiment on this subject. In using his two cultures, one isolated from a Racoon (Nasua) the other from a bull he observed that in the one case(that of the culture from the bull) the infected rabbit succumbed on the 16th day after inoculation and the lungs were studded with tuberculous foci. The rabbit inoculated with the other strain, however, did not die, but was killed after 56 days and found practically healthy. VAGEDES (11) very soon afterwards was able to confirm this observation by demonstrating the high virulence which fresh bovine viruses possess for rabbits even in minute doses.

Since then it has been abundantly proved that for the differentiation of the two types of tubercle bacillus, rabbits serve just as useful a purpose as calves.

As the outcome of an extensive series of experiments/

experiments the ROYAL COMMISSION (7) came to the conclusion that "The results produced by injecting the bovine tubercle bacillus into calves and rabbits in the above doses are thus very striking and definite, and taken with the cultural characters of the bacillus afford a trustworthy means of recognising the bovine tubercle bacillus. Indeed, as our investigation progressed we found that it was sufficient to inoculate rabbits for differential diagnosis" - - - - "Tubercle bacilli which are highly virulent for the rabbit always proved highly virulent for the calf, and tubercle bacilli which produced in the rabbit retrogressive tuberculosis never produced in calves more than a limited retrogressive tuberculosis".

Again PARK and KRUMWIEDE (1) working on the same lines found that rabbit is the best animal to use for testing virulence for diagnosis of the type of tubercle bacillus.

The important fact was thus established that with the rabbit alone one is able to distinguish with certainty the bovine from the human tubercle bacillus.

MODE/

MODE of INJECTION and DOSAGE.

In the use of rabbits as a means of differential diagnosis four methods of inoculation can be employed, intra-articular, subcutaneous, intra-peritoneal, and intravenous.

1. The intra-articular method of injection for the differentiation between the human and bovine types of tubercle bacilli was introduced by FRASER (2). He has chosen the knee joint of the rabbit as being the most convenient and accessible and, in his opinion, the ideal situation is the synovial membrane in which to demonstrate the distinctions between the two types of tubercle bacilli. The test is judged by the degree of reaction, clinical and pathological, consequent upon inoculation of the joint with 1 ccm. of bacillary emulsion.

2. The sub-cutaneous method has the disadvantage that the local lesion may ulcerate and infective material may be discharged, leading to sinus formation and to the contamination of the surroundings.

3. The intra-peritoneal injection would not have/

have this objection, but it takes longer time for the animal to show indications of the disease and, in this respect, is not equal to the fourth method.

4. The intra-venous method. The ROYAL COMMISSION (8) are of the opinion that for an intravenous injection into the rabbits for purpose of identification a dose of 0·01 mgm. should be used. This dose and mode of inoculation were, in part, also adopted by, among others, FRASER (2) and MITCHELL (12).

I have employed throughout the course of my investigation for purpose of identification, the intravenous mode of inoculation, using 0·01 mgm. of dried culture as the dose, and rabbits were used for economic and other reasons. Every strain of cultures isolated has been subjected to this test, and its result along with cultural characters was accepted as the basis of differentiation. Further, wherever a strain had been demonstrated by the first rabbit injection to be of the bovine type, this result was again corroborated by a second rabbit injection.

The weight of the rabbit before inoculation was taken and recorded, and also that at death. If possible, rabbits weighing between 1000 and 2000 grammes/

grammes were employed, but those of other weights have also been utilised, and my experience failed to detect any appreciable difference on the pathological findings caused by variation in size of the animals; if anything, the small sized rabbits seemed to have better answered the purpose.

Reliance has been placed on the macroscopic inspection of the lesions for differentiation; but, in this respect, there is the possibility of pseudo-tuberculosis being mistaken for tuberculosis. This can, however, be avoided by remembering the fact that pseudo-tuberculosis chiefly affects the vermiform appendix, the glands, the spleen and the liver - rarely the lung. Further it can easily be differentiated by making films from the nodules.

Each of the two types of tubercle bacilli produces distinct and different changes on rabbits.

I. In the first instance, a rabbit injected intravenously with a dose of 0·01 mgm. of tubercle bacilli of the bovine type presents the following characteristics. The animal loses weight, sometimes even to the extent of half of its initial weight, and almost invariably succumbs within 6 weeks after inoculation to a rapidly fatal tuberculosis. On autopsy/

autopsy:-

THE LUNGS are very voluminous and almost completely fill the chest. They are studded throughout with tubercles or masses of varying sizes; these are often large as the result of the confluence of smaller tubercles, forming grey caseating nodules.

THE SPLEEN is enlarged, sometimes extremely so, and closely beset with caseating tubercles.

THE LIVER may be moderately enlarged and commonly shows, scattered through its substance, numerous small greyish yellow tubercles.

THE KIDNEYS often, though not invariably, become the seat of many grey or caseating miliary tubercles.

THE LYMPHATIC GLANDS are always affected, more particularly those of the Bronchi and Axilla, and show large tubercles with central caseation.

II. On the other hand, a rabbit inoculated with the same dose of the human tubercle bacilli, under identical conditions as regards weight and mode of administration, never dies of tuberculosis within 3 months; if death does occur within this time, it is/

is due to causes other than tuberculosis. The animal generally lives for a long period of time and, if killed at the end of 3 or 4 months, is often found in good health and not infrequently has increased in weight.

THE LUNGS in such cases very usually are collapsed, and fall away from the chest wall, when this is opened. They either show no tuberculosis or at most a small number of scattered grey tubercles already infiltrated with fibrosis or calcification; some of these may occasionally develop into nodules with caseous foci in the centre. The rest of the organ is crepitant and comparatively healthy.

THE SPLEEN is seldom enlarged and rarely, if ever, affected with tuberculous nodules.

THE LIVER also rarely shows any tubercles.

THE KIDNEYS are involved in the majority of cases and generally show in the cortex a few grey miliary tubercles, some with caseous foci in the centre.

THE LYMPHATIC GLANDS are very seldom affected.

CONCLUSIONS/

CONCLUSIONS.

As the outcome of a series of inoculation into rabbits performed during the experimental investigation of the cases tabulated in the earlier part of this paper and taking the facts already outlined into consideration together with those observed by other workers, the conclusion can safely be drawn that by means of the rabbit test alone, tubercle bacilli as they occur in lesions in human beings can be divided into two distinct groups. One group possesses identical cultural characters and virulence for rabbits with those exhibited by tubercle bacilli isolated from bovines and may be thus termed the bovine type; the other group has a low virulence for rabbits, is practically always obtained from human sources and may be termed the human type.

MORPHOLOGY/

MORPHOLOGY.

As usually described, the tubercle bacillus is an organism measuring about 3 μ. in length and .3 μ. in breadth. This is generally true when applied to the bacillus found in animal tissues, but, under artificial conditions, its size varies within wide limits. Such variation depends on the type of tubercle bacillus concerned, the age of the culture from which it is observed, and the kind of medium on which it is grown.

SMITH (1) in his first communication, pointed out the morphological distinction between the human and the bovine types of tubercle bacillus, when grown on blood serum. The human bacillus, according to his description, is long,(about 3 μ.)curved, slender, and less uniformly stained, whereas the bovine type is shorter (about 1 μ.) and deeply stained.

VAGEDES (2) also observed that tubercle bacillus of the bovine type is generally shorter when grown on blood serum.

RAVENAL (3) working with glycerine agar

also/

also noticed the same distinction.

WOLBACH and ERNEST (4) found practically no such differences on egg medium, but admitted that on serum and glycerine agar there was, however, some slight dissimilarity, the bovine on the average being shorter. On broth both human and bovine assumed a longer form, the former tending to be longer.

KOSSEL, WEBER and HEUSS (5) also recognised such a morphological distinction between the two types in freshly isolated cultures when grown in bouillon under identical conditions; the human bacillus is usually slender, regular in shape and long, while the bovine bacillus is thicker and more squat in shape.

Similarly the BRITISH ROYAL COMMISSION (6) found that the human tubercle bacillus, when grown on suitable media is, on the whole, longer, varies more in length, and is less resularly straight and less uniformly stained.

PARK and KRUMWIEDE (7) also took cognizance of such morphological variations between these two types. Cultures have been examined by them at various generations of their growth and they found that/

that the tendency was for the human type to show longer forms and for the bovine to show shorter forms in the later generations.

Such differences in morphological characters have also been commented on by RABINOWITSCH (8) and FIBIGER and JENSEN (9); but all authors, though recognising these general distinctions, consider them too inconstant to be of any practical value in the identification of the type of tubercle bacillus.

OWN OBSERVATIONS. For this purpose I have restricted myself to the use of egg medium, with and without the addition of glycerine. Films were made from cultures at various generations of their growth, stained by Ziehl-Neelsen in the same way throughout, and examined. In all, 30 strains of the human and 12 strains of the bovine type have been so prepared and examined at their various stages of growth, and, while differences in their morphological characters were observed on both kinds of media, they were specially evident in the case when glycerine egg was employed. So little marked were they on the plain egg/

egg medium and so marked were they, comparatively speaking, on the glycerine medium, that I have confined myself to recording the differences on this latter medium.

In the first or second generation of their growth, sub-cultures being made once about every three weeks, there were no appreciable morphological distinctions, but in the later generations it was possible in a certain proportion of cases to recognise and to distinguish the types to which the virus belonged. The human strains, on the whole, showed longer and slender forms, and were generally unevenly stained.

My results give for the human type, when observation was made at the 5th generation, 28% long and 26% short forms; for the bovine type over 50% showed short forms, while practically none belonged to the long type. Regarding their staining properties, stained under identical conditions, 65% of the human were unevenly stained against 20% of the bovine type.

The following TABLE gives a comparison of my results with those of PARK and KRUMWIEDE (7).

5th/

TABLE VII.

5th GENERATION of GROWTH.

MORPHOLOGICAL CHARACTERS.

OWN OBSERVATION	LONG	MEDIUM	SHORT.
Human	28%	46%	26%
Bovine	1% ?	45%	54%
PARK & KRUMWIEDE			
Human	33%	50%	17%
Bovine	0%	50%	50%

STAINING CHARACTERS.

		EVENLY STAINED	UNEVENLY STAINED
OWN OBSERVATION	Human	35%	65%
	Bovine	80%	20%
PARK & KRUMWIEDE	Human	20%	80%
	Bovine	75%	25%

It/

It becomes evident, therefore, from the figures above quoted that where difference exists, it is only relative and present only in a certain proportion of cultures. Diagnosis of the type of virus, on the strength of microscopic examination alone, can only be provisional, since the distinction, if present, is not sufficiently marked and constant to be of any real practical utility. Virtually all observers are agreed that the value of such morphological variation is very restricted and none have attached any great importance to it in the identification of the type of tubercle bacillus, without, at the same time taking into consideration the cultural and other biological tests.

CULTURAL CHARACTERS.

SMITH (1) was the first to attempt to use the cultural characteristics of the two types as a means of differentiation. Cultures obtained from two different sources were made use of, one being isolated from an animal related to the Racoon (Nasua Narica) which had succumbed to tuberculosis, the other from a bull suffering from tuberculosis of some standing. Blood serum was employed by him. The growth on this medium of the one which proved to be of the human type was abundant, while that given by the bovine strain was very sparing. Two years later he (2) again further differentiated the bovine from the human bacillus, and showed that they were heterogenous in cultural character and in virulence, whereby it was possible to recognise them.

In 1903, making use of glycerine bouillon as the medium he (3) also noticed that, in addition to the qualitative differences between the character of the growth of the human and that of the bovine type, there were distinctive disparities in the amount of the acid and alkaline production on this medium/

medium by the two types. The human type after causing an initial drop in the acidity of the medium to nearly normal, increased the acidity in the later stages, until it again approached or slightly exceeded the original reaction. On the other hand, the bovine type rendered the medium less acid, and ultimately the reaction with this organism might even become alkaline.

A year later he (4) further pointed out the use of his Reaction Curve method as a basis of bringing out the difference between the two types. At least 3% glycerine should be added to the broth, and the titre of the glycerine bouillon in which the tubercle bacilli are growing estimated from time to time gives this curve.

On the result of more extensive experiments, he (5) further demonstrated the importance of the reaction curve in 5% glycerine bouillon in the studies of the type of tubercle bacillus.

Using the Reaction Curve method upon twelve strains of Avian, four Human, and one Bovine, BANG (6) was able to confirm the results obtained by Smith.

This/

This test, however, has been found less useful in the hands of other observers. GRUND (7), while not denying that the Glycerine Reaction Curve is undoubtedly valuable, corroborative evidence of a division of tubercle bacillus into two types, found that its value is lessened by a number of irregular and atypical reactions encountered; while as a practical aid in determining the type of an individual virus, it is also much handicapped by the length of time required for the experiment.

Similar difficulties have also been experienced by DUVAL (8) and LEWIS (9) who found some atypical strains which conform to neither the bovine nor the human type.

THE ROYAL COMMISSION (10) on the result of an extensive study of this test, express the following opinion:-

> "the formation of free acid or alkaline is only a subsidiary event in the life history of the bacillus and cannot be made the basis of any fundamental distinction" . . . . . "It is merely a striking indication of luxuriance of growth and we cannot deduce from it more than we can from the/

the luxuriance of growth itself" . . . . "The extent, however, to which the acidity is lowered by the one type of bacillus or raised by the other has shown such variation that no clear distinction in bio-chemical properties appears between the two groups of bacilli".

When the amount of growth, rather than the acidity produced is considered, it cannot be doubted that the addition of glycerine gives a practicable and efficient method of identifying the two types of tubercle bacilli in a large majority of instances.

MOELLER (11) was one of the first to notice that the presence of glycerine had, as a rule, a restraining influence on the growth of a fresh bovine culture.

KOSSEL, WEBER & HEUSS (12), using freshly isolated cultures, observed that on glycerine bouillon the human type grew well, usually covering the surface completely in 2 or 3 weeks, and forming a uniform wrinkled membrane; with the bovine the growth was much slower and scanty, consisting of only a thin fine follicle.

OELECKER(13) and DIETERLEN (14), among others, also agree that the addition of glycerine has a restraining influence on the growth of the bovine/

bovine tubercle bacillus. This influence of glycerine is not confined to an effect on the quantity of cultural growth but may also bring out distinctions in the characters of colonies produced on suitable solid media. This was the experience of PARK and KRUMWIEDE (15), and others, who noticed that on glycerine egg bovine tubercle bacilli usually form isolated colonies and rarely an almost complete layer; the tendency for the growth to acquire a moist character is also a very distinguishing feature of the bovine type. The human type, however, grows luxuriantly from the start and, if discrete, the colonies are generally large and rounded. When confluent, the growth is raised, crumpled or coarsely verrucose, and assumes a dry appearance.

OWN OBSERVATION.

From the preceding sketch of some of the work already done by previous investigators, it becomes intelligible that the most marked and more or less constant difference experienced is in the amount of growth of the two types. Directly dependent on this, there is also the difference in the reaction curves when the bacilli are grown in glycerine/

glycerine broth. As regards the latter process, the difficulty of the method, the uncertainty of the medium, (as not all batches of the same medium are suitable for the differentiation), the time for incubation, together with the large number of cultures which are required for the test are objections which preclude one from adopting this method to any great extent.

Further, in connection with this test, there is often the difficulty of getting a good surface growth by the use of such techniques as growing on cork, a fact which has been pointed out to me by Dr. McGOWAN (private communication); but, by the method introduced by him of obtaining an abundant surface growth on feathers saturated with a thick emulsion of the tubercle bacilli, this difficulty is largely overcome.

It is not the primary intention of the present work to discuss or to consider at length the merit of the cultural characters as a means of distinguishing the type of tubercle bacillus, but, as in the course of investigation some such opportunities incidentally presented themselves, some records of the observation made may be given. In doing so, I have to confine myself to those based on the study of/

of the behaviour of tubercle bacilli on plain and glycerine egg media, as these were almost exclusively used throughout. The terms "Dysgonic" and "Eugonic", (employed by the BRITISH ROYAL COMMISSIONERS (10) to denote respectively that the bacillus grows with difficulty or with readiness on a medium or on several media) appropriately express the characteristics exhibited, in most cases, by the bovine type in the former and by the human in the latter case. It should be stated that, while such cultural differences as exist between the two types can be observed on most of the suitable media, they become more marked when glycerine is present as one of the constituents of the medium employed.

The human tubercle bacillus on plain egg grows more rapidly and luxuriantly than does the bovine type, the colonies, when numerous, becoming visible to the unaided naked eye within the first ten days or first fortnight; when sparse, their appearance may be delayed until the third week. When grown on glycerine egg, the difference between the growths of the two types is even more apparent and, in addition, the human type growth has a characteristic/

characteristic wrinkled appearance and a tendency in some cases to become pigmented.

In the case of the bovine tubercle bacillus, the growth does not appear until the third week; usually its appearance is even later than this. On glycerine egg one of the characteristic and almost constant features of the growth, if present, is the tendency to acquire a moist surface, As a rule the colonies do not show pigmentation:- at all events, in the primary and in the first few generations - &, instead of having a wrinkled surface, they form a thin greyish uniform layer of growth. Often primary cultures of this type fail to develop on glycerine egg, but, after prolonged growth on this medium and when they have become accustomed to the glycerine, their growth tends to an increasing luxuriance and ultimately loses its distinguishing feature.

The routine method, I employed, was to inoculate a small piece of the tuberculous tissue (obtained from the inoculated guinea-pig) on plain as well as on glycerine egg medium and to observe the growth at the end of the second or third week.

The results of my experience have led to the/

the following conclusions.

1. All primary cultures growing rapidly and luxuriantly on glycerine egg are of the human type. The only possibility of error in this respect is that the culture may contain a mixed strain of human and bovine tubercle bacilli.

2. All primary cultures growing comparatively slowly and less vigorously on plain egg medium, and sparingly or not at all on glycerine egg, with a tendency to assume a moist appearance, are in almost all cases of the bovine type, provided one is not dealing then with an atypical strain (which does, though rarely occur.)

PORTAL OF ENTRY.

Since a human and a bovine type of tubercle bacillus have been recognised, and since either is found capable of infecting man, it would be interesting to record some of the more important views with respect to the channels of infection taken by these two types of bacillus, and as to how far these views agree with the post mortem and other evidence.

Generally speaking, the paths by which it is possible that tubercle bacilli may gain entrance into the body are:-

I. By way of the Skin.
II. By heriditary transmission.
III. By inhalation.
IV. By ingestion.

I. CUTANEOUS INOCULATION.

Villemin, by experiment, in 1865 was the first to demonstrate the infective nature of the disease on inoculation. This mode of infection is most commonly seen in persons whose occupation brings them/

them in contact with dead bodies or animal products, as pathologists, butchers etc. Other means of cutaneous inoculation have been described but it may be said, that on the whole, infection by this path plays but a trifling role in the transmission of tuberculosis.

II. HEREDITY.

The theory of infection through heredity finds few supporters. In order that the disease could be so transmitted from the male, it would be necessary that the tubercle bacillus either should lodge in the individual spermatozoon which fecundates the ovum, or should be present in the seminal fluid, (not necessarily in the spermatozoon) and ultimately infect the ovum. Infection from the female involves the question of transmission through a fertilised ovum invaded with a tubercle bacillus, independent of an infection conveyed by the spermatozoon, and also the question of infection originating from a tuberculous placenta or due to tubercle bacilli circulating in the mother's blood, and gaining access into the foetal circulation.

The most prominent upholder of this hereditary theory is Baumgarten (1) who believes that the bacilli can be conveyed to the subject during intra-uterine development and claims that in one instance he has been able to demonstrate the presence of tubercle/

tubercle bacillus in the ovum of a female rabbit which had been artificially fertilised with tuberculous semen. His hypothesis is based on two main factors, namely, the great frequency of the disease in early life and the localisation of the tuberculous lesions in childhood. He assumes that the tuberculous bacilli lie inert in the body of infants, and under suitable conditions as in a lower resistance of the individual, subsequently multiply.

The possibility of such transmission is admitted by, among others, EMRYS ROBERTS (2) and KOSSEL (3). Most authorities, however, deny that this is a common or important means of infection and consider that the percentage of cases of congenital tuberculosis is extremely small. That tuberculosis claims victims in one generation after the other in some families is due in all probability to infection being rendered much more possible from the infected surroundings, and possibly, from a predisposition to the disease produced by an inherited low power of resistance which offers an easy path for invasion by the tubercle bacilli

III./

III. INHALATION.

KOCH (4), while he erred in ignoring the intestinal path of entry of tuberculous infection, rightly considered the respiratory tract as an important channel for the tubercle bacilli gaining access to the body. In his famous address before the Conference on Tuberculosis in London, he gave it as his opinion that . . . . . ."in by far the majority of cases of tuberculosis, the disease has its seat in the lungs, and has also begun there. From this fact, it is justly concluded that the germs of the disease, that is the tubercle bacilli, must have got into the lungs by inhalation" . . . . . "On the contrary, we know with certainty that they get into the air with the sputum of consumptive patients" . . . . "The sputum of consumptive people, then, is to be regarded as the main source of the infection of tuberculosis".

This is in agreement with the extensive experiments conducted by CORNET (5) which afford indisputable evidence that the dust of a room or other locality frequented by patients suffering from pulmonary/

pulmonary tuberculosis is capable of carrying infection. He lays special stress on the importance of fine particles of dust as carriers of the bacilli which, on being inhaled, gain entrance to the system through the lungs.

WOODHEAD (6) is also of the opinion that the lungs are very frequently the channel of infection.

Similar views are entertained by BARTEL and NEUMANN (7) who believe that air borne bacilli freely enter the air passages and get carried to the lungs.

FINDEL (8), as the result of his experiments on dogs and guinea-pigs shows that all things being equal, a dose 1220 times as large as that required to produce tuberculosis of the lung has no effect when administered by way of the digestive tract.

These and other evidences demonstrate that the aerogenic route of tuberculous infection plays an important part in the spreading of the disease, and most authorities now agree that the tubercle bacilli enter the body most easily and most frequently through some part of the respiratory part, at least in so far as/

as adult persons are concerned.

There is however, as yet a divergence of opinion as to whether the lungs or the bronchial and hilus glands are primarily affected.

RIBBERT (9) while acknowledging that tuberculous infection is aerogenic, asserts that the lung lesion is not primary but secondary to an affection of the tracheo-bronchial glands.

The bacilli, he believes collect there, and ultimately gain access to the blood, pass through the pulmonary vessels, and are arrested mainly in the apices of the lungs.

This view was subsequently supported by WELEMINSKY (10), who stated that the tubercle bacilli having lodged in the bronchial glands were carried from there to the lungs, through the blood stream.

LAPAGE (11) also believes that in children pulmonary tuberculosis usually starts at the roots and is disseminated therefrom to the lungs.

SLUKA (12), basing his views on X-ray evidence has pointed out that there is at first an enlargement of the bronchial glands and subsequently the invasion spreads to the lungs.

On/

On evidence of a similar nature a like opinion is held by JORDAN (13) who regards phthisis as a primary disease of the root glands.

Among those accepting this doctrine are:- LEON (14), STOLL (15), LESLIE (16), and BYTHELL (17). All these have assured themselves that it is the hilus and not the apex of the lung which in general, shows the primary focus of the disease, certainly in children and probably also in adults.

It would appear therefore that there exists a great deal of evidence for the infection of the lungs taking place by a spread from the bronchial and hilus glands. But indirect contradiction to this conception is the work of GHON and ROMAN (18) who claim to have established the fact by examination of a series of autopsies on children that with the exception of a small number of cases, a primary infection of the lungs themselves can be demonstrated.

It would appear impossible, therefore, to reconcile these opposing views, and it is probably inadvisable to attempt to draw a hard and fast conclusion. The writers who uphold the primary lung infection/

infection theory would seem to have ignored the physiological influence of respiration on the thoracic lymph flow. It has been pointed out by RITCHIE (19) that, as each respiratory movement helps to fill the heart, so a corresponding suction may occur from the lymphatic glands that surround the lung. This should have an important effect in the tuberculous infection of the organ. Another important factor is that the bronchial glands receive the lymph drained from distant parts of the body as well as that directly from the entire surface of both lungs.

On these two accounts, therefore, they are afforded a greater opportunity of being infected and should there be any lymphatic obstruction taking place by reason of their becoming either diseased or hypertrophied, an impediment to the normal flow of lymph results. It is quite conceivable, then, that in a more or less limited area the obstructed lymph current may be reversed and encouraged by the act of respiration, deposit whatever germs it then carries, centrifugally and collaterally, thus rendering it possible for the infective inoculum to produce a disease of the lung.

IV. INGESTION.

In this connection, the portals of entry for the tubercle bacilli may be:-

A. The Tonsils and their adjacent glands.

B. The Intestines.

I will now consider some of the more recent views with reference to the possibility of these paths acting as a channel of infection in tuberculosis.

A. THE TONSILS and their ADJACENT GLANDS.

The path of entry through the tonsils and the lymphoid tissues of the naso-pharynx in tuberculous disease in children, and the frequency of involvement has been sufficiently recognised by many observers.

STILES (21) lays great emphasis on the importance of the tonsils as a portal to the cervical glands whence the tubercle bacilli are carried to the right side of the heart by first gaining access to the interior of the small veins connected with them.

A similar opinion arrived at from clinical considerations is that of PHILIP (22) who regards the tonsils and extratonsillar glands as a common path of invasion/

invasion.

MITCHELL (23) in his study of 72 clinical cases of tuberculous cervical adenitis found that in 37.5 % the tonsils showed histological evidence of tuberculosis.

Corroboration is also found in the experience of FRASER (24) who, basing his view on the observation of 300 clinical cases of tuberculous cervical adenitis, has pointed out the importance of the tonsils as a common site of entry.

Others who consider the channel of importance as regards the entry of tubercle bacilli in children are FORDYCE and CARMICHAEL (25) and PYLUS (26).

B. THE INTESTINES.

A primary infection of the intestine was considered of so rare an occurrence by KOCH (4) that he did not recognise this portal of entry as of any importance. He based his opinion on the fact that amongst 933 cases of tuberculosis in children at the Emperor and Empress Friedrich's Hospital for Children in Berlin not a single case of tuberculosis of the intestine was demonstrated without at the same time a simultaneous/

simultaneous disease of the lungs and the bronchial glands; in support of his contention he further quoted Biedert's observation that out of 3,104 cases only 16 were of primary tuberculosis of the intestine. He states "That a case of tuberculosis has been caused by aliments can be assured with certainty only when the intestine suffers first, that is, when a so-called primary tuberculosis of the intestine is found. But such cases are extremely rare".

On account of the importance of this subject many experiments have since been conducted in this direction by various investigators, foremost of all perhaps are the ROYAL COMMISSIONERS (20). Quoting their words . . . . . .

> "There can be no doubt that a considerable proportion of tuberculosis affecting children is of bovine origin, more particularly that which affects primarily the abdominal organs and the cervical glands".

At this juncture mention may be made that out of 59 of my unselected cases, other than sputum, 18 were affected primarily in the intestine.

From a balancing of the evidence and from my own experience a conclusion may therefore be drawn that primary infection through the alimentary tract does/

does occur and that it is found more especially in children consuming milk or other food contaminated with tubercle bacilli.

QUESTION of PULMONARY TUBERCULOSIS being CAUSED by INGESTION

As the subjects of infection by inhalation and ingestion have just been treated of, it is opportune to discuss a further question in relation to both about which there is considerable dispute.

In direct contradiction to the view of KOCH is that of BEHRING (27) who announced in 1903 at the Naturforscher Versammlung in Kassel that pulmonary tuberculosis has its origin in the alimentary tract and that the seeds of phthisis are laid in infancy through the intestinal mucosa. The infection, according to his view, is conveyed to the infants through milk and remains latent until the power of resistance happens to be impaired at some later period of life. The disease then takes on an active form.

This hypothesis finds the support of RAVENAL (28) who produced pulmonary tuberculosis in animals by feeding experiments.

Further corroboration seems to have been afforded by the experiments of Vansteenberghe and Grysez (29) who produced anthracosia of the lungs of guinea-pigs/

guinea-pigs by introducing china ink emulsion into the stomach, the carbon particles being absorbed from the intestine by the lymphatics into the blood and thence to the lungs. They also submitted young and adult guinea-pigs to the test and found remarkable difference of results between them. In the former, the carbon particles were filtered out by the mesenteric glands while the lungs remained free; in the latter, though the glands suffered no affection, the lungs were already carbonized. They further demonstrated that authracosis is not produced by making the animals breathe an atmosphere saturated with soot so long as they are prevented from swallowing the accumulations in the nose and pharynx.

CALMETTE and GUERIN (30) following RAVENAL's experiments but with improved technique have shown that the lungs may be easily infected through the intestinal route, leaving only a trace of the disease in the bowel and, on the results of their experiments, assert that the majority of cases of pulmonary tuberculosis originate in this manner. They fed adult goats with bovine tubercle bacilli and found that they contracted severe lung tuberculosis, and conclude that adult/

adult animals may readily contract pulmonary tuberculosis when virulent bacilli are introduced into the digestive tract. They, however, differ from Behring's view in that they consider that the adult is more susceptible to pulmonary infection by the intestinal route than the infant.

WHITLA (31) on the results of a series of experiments on guinea-pigs and rabbits with carbon particles and china ink found that absorption readily takes place through the intestinal epithelial surface. The particles having reached the lacteal or lymphatic paths then pass to the lymphatic glands of the mesentery. Either free or enclosed in phagocytes, they then find their way into the thoracic duct to be carried to the venous circulation before being finally arrested in the pulmonary capillaries.

The experiments of these writers and the conclusions arrived at by them were, however, severely criticised by COBBETT (32) who ably pointed out the many errors committed by the supporters of Behring's theory.

On the result of many experiments he comes to the following conclusions, amongst others:-

"Feeding/

"Feeding with finely divided carbon does not cause pigmentation of the mesenteric or other lymph glands of guinea-pigs . . . . . neither does it cause pigmentation of the lungs or bronchial glands of these animals, either young or old . . . Pulmonary tuberculosis in the guinea-pigs can be readily caused experimentally by inhalation of, but not by feeding with, the tubercle bacilli. These experiments lend no support to the theory that the intestine furnishes a common portal of entry for the tubercle bacilli which causes phthisis".

From the foregoing, it will be noticed that there is a possibility that the tubercle bacilli may gain entrance into the body by the cutaneous, hereditary, respiratory or alimentary route. With regard to the possibility of infection by the skin and hereditary routes, most authorities are agreed that this seldom takes place. They further are of the opinion that the most common portals of entry are by way/

way of the respiratory and alimentary tracts. The question as to which is the important channel of invasion in tuberculosis of the lungs and their regional glands (bronchial and root glands) has been much in dispute of recent years, and experiments directed to a solution of this problem performed by different investigators give diametrically opposite results. Seeing that the lungs are the organs of the body most frequently affected, it is not difficult to conceive that the most popular theory of the channels of infection would be that of the respiratory passages and that primary pulmonary tuberculosis was the direct result of an air borne infection. This view was not challenged until 1903, when von Behring put forward the view that pulmonary tuberculosis is frequently caused by the virus having been ingested and absorbed from the intestine, and that the bacilli so absorbed are capable of lying in an inert condition for a long time and may, at one period or another, be carried to the lungs there giving rise to pulmonary tuberculosis.

Now if Behring's hypothesis be accepted, it should follow:-

I./

1. That the tubercle bacilli isolated from cases of pulmonary tuberculosis should be of the bovine type or, if human, we must infer that a complete metamorphosis of the bacilli has taken place from one type to the other under the natural conditions in the living body. For, according to this theory, the infection contracted in early life through the consumption of contaminated milk, via the alimentary canal, may remain latent for years and then in adolescent or early adult life, under suitable conditions, may develop and give rise to the clinical signs and symptoms of pulmonary tuberculosis.

2. That if, in primary pulmonary tuberculosis, the infective agent is carried to the lung in the blood stream as alleged by the supporters of this theory, then we should expect to find in the great majority of cases the two lungs and their regional glands affected to an approximately equal extent, and

3./

3. That old calcareous or caseo-calcareous glands so often found in the mesentery, (though they do not owe their origin in all cases to an infection with the tubercle bacillus) and also the glands, (even apparently normal in appearance), draining the areas of absorption in the intestine, should, as a rule, if injected into susceptible animals produce tuberculosis.

With regard to the provisional conclusion No. 1 based on Von Behring's theory, one finds, that out of 1,044 cases of pulmonary tuberculosis in persons of all ages collected in the literature, (vide infra) bacilli of the bovine type. were found in only 6 instances. If, therefore, Von Behring's view be correct, it must be assumed that the bacilli while in the body have undergone a change of type, from bovine to human. Among those in favour of such transformation is EBER (33) who in an extensive investigation succeeded in infecting calves from 3 cases of human pulmonary tuberculosis. The bacilli used for the experiment were isolated from human material and were of the human type, but after passage through the calf, they/

they, however, assumed the character of the bovine type. DAMMANN and MUSSEMEIER (34) also claimed to have succeeded in changing a human type to a bovine by passage through a series of goats.

But there is an overwhelming majority of workers on this subject whose experiments do not support this contention. Quoting the ROYAL COMMISSION (20) :-

> "The results of the experiments detailed in this report lend little support to the surmise that modification of the recognised types of bacilli can be experimentally induced by passage through animals".
> Again, "The passage experiments performed since the 2nd Interim Report lend no support to the view that the human tubercle bacilli can be changed into bovine tubercle bacilli by passage through the bodies of calves or other animals".

KOSSEL, (3) made several very thorough experiments but he did not obtain any change of the human type of bacilli into the bovine type in the bodies of rabbits, cattle and goats. An identical result/

result was obtained by WEBER (35) in that a culture of tubercle bacilli of the human type was passed through cattle for 685 days but did not suffer any change. OEHLECKER (36) also could not detect any transformation of type by passage through animals.

Such negative results are also obtained when the tubercle bacilli are grown in artificial media for a prolonged period. Thus the ROYAL COMMISSION (20) have not found that bovine tubercle bacilli diminished in virulence to any great extent when subcultured for long periods, in one instance for as long as 1,487 days. In two of my own bovine cultures, no alternation in virulence for rabbits was noticed after a continuous growth in egg medium, in one case for 758 days and in the other for 752 days.

Against the second provisional conclusion the statistics collected by SHENNAN (37) may be quoted. Out of 183 cases he found that in 123, or 67.2%, the bronchial glands on the right side were alone or more affected; and again in 60, or 32·8% those on the left side showed either a more advanced tuberculosis or were alone affected.

With/

With respect to the third provisional conclusion one may mention the fact that, in experiments conducted by other workers and myself, (vide infra), in the great majority of cases(90%) the apparently normal or otherwise enlarged glands in the mesentery in both children and adults failed to produce tuberculosis in guinea-pigs on injection; while in the case of calcareous or caseo-calcareous glands, though a greater number of positive results were obtained, one nevertheless did not find such a percentage of infection in the inoculated animals as one would expect if Behring's theory be regarded as universally true. If this hypothesis were accepted, one should find that such glands, harbouring in most cases as they are supposed to do, tubercle bacilli in a latent form, should be able as a rule, if not invariably, to give infection to so susceptible an animal as the guinea-pig. Their failure to do so in so many instances points to the fact that either they are not so generally infected with the tubercle bacilli as Behring's view would lead us to believe, or the tendency of the virus in the living animal tissues is to perish in many/

many cases in retrogressive lesions.

While admitting that latent tuberculous infection in the human body does occur in a certain Proportion of cases (vide infra), one is inclined to come to the conclusion that the theory, that pulmonary tuberculosis is the result of an infection contracted during early life by way of the intestine, has not been substantially proved & cannot be accepted without further more convincing evidence. But in rejecting this theory as being too comprehensive one must, by no means, exclude the possibility of such a path of invasion in certain cases of pulmonary tuberculosis, for among those who recognised this portal of entry whereby the lung is affected are The ROYAL COMMISSION (20) RIVIÈRE (38) RAVENAL (28) JORDAN (13) COBBETT (32) and EMRYS ROBERTS (2).

The channel by which such a transmission of infection could take place corresponds, according to CULLEN (39), to the path of the lymph flow, from the lymphatics of the intestine passing <u>en route</u> the mesenteric glands and along the receptaculum Chyli finally ending into the left subclavian vein <u>via</u> the thoracic duct. JONES (40) has traced a similar path by which matter absorbed from the intestines could finally lodge in the lungs.

LATENT/

LATENT TUBERCULOSIS.

When one speaks of latent tubercle bacilli one means such bacilli as are residing in a tissue without producing a specific tissue change, that is, a new formation or change of tissue which possesses the well known characteristic structure of the tubercle.

ORTH. (1) as early as 1879 pointed out that glands though normal in appearance to the naked eye may show tuberculous changes on histological examination, and he was the first to demonstrate the existence of such lesions in the tissues of the human body in conditions where they were undetected by the unaided eye.

This view was subsequently corroborated by LOOMIS (2) who demonstrated that glands which did not present to the naked eye any evidence of disease and were therefore considered normal could cause a tuberculous infection in animals. He used for his experiments the bronchial glands from adults.

In the following year further confirmation was found in the investigation of PIZZINI (3) who showed that out of 30 cases of adults, in whom no tuberculous/

tuberculous lesions could be ascertained, 12 (10 with the bronchial and 2 with the bronchial and cervical glands) were found infected with tubercle bacilli on injecting the glands into animals.

EASTWOOD AND GRIFFITH (4) in the course of their investigation into the incidence and bacteriological characters of tuberculous infection in children have studied 150 cases in children. Among these were 61 cases showing at the post mortem examination neither evidence of infection with tubercle bacilli nor visible lesions of tuberculosis. In every case, excepting one, (in which the cervical glands were also included) the bronchial and mesenteric glands were separately studied by inoculating each group into guinea-pigs. Of the 61 non-tuberculous cases, 5 produced tuberculosis in the inoculated animals, the tubercle bacilli isolated being of the bovine type in three instances.

STANLEY GRIFFITH (5) has also studied by means of animal inoculation the bronchial and mesenteric glands of 33 children who showed at autopsy no macroscopic evidence of tuberculosis. In one of 2 further cases the bronchial glands alone, and in the other/

other the mesenteric glands alone were investigated. Exclusive of one case in which all the guinea-pigs inoculated died prematurely, out of the groups of glands belonging to 34 children, two produced tuberculosis in the guinea-pigs inoculated, and in each instance it was the bronchial gland group. The cultures obtained from two cases were found to possess the cultural characters of the human tubercle bacillus and were of low virulence for the rabbit.

Unfortunately no histological examination of the glands was undertaken by the last four observers, so one cannot speak of their cases, with any degree of certainty, as latent tuberculosis in the strict sense of the word.

Our first definite knowledge of the occurrence of latent tuberculosis appears in the communication of KAEBLE (6) who mentions that two cases out of 23, in which the bronchial glands were used for the inoculation, gave positive results.

Not long afterwards, this subject was further investigated by MACFADYEAN AND MACCONKEY (7) who examined a series of mesenteric glands from 28 post mortem cases all of which, excepting one of 6 and another of 8 years old, were under 5 years of age/

age. The 28 cases, based on a gross examination at autopsy, were divided into 2 groups, tuberculous and non-tuberculous, the former numbering 8 cases, while the latter numbered 20. Of the non-tuberculous cases 5 were proved tuberculous on animal experiment, and in two of these a histological examination did not demonstrate the presence of any tuberculous lesions.

Since then more investigations on this subject have been recorded. ROSENBERGER (8), in his inquiry involving a study of the mesenteric glands in 21 non-tuberculous cases which showed no tuberculous changes histologically, found that, 6 (4 adults and 2 children) out of 14 cases were capable of conveying tuberculosis to experimented animals. The percentage may be greater, however, as some of the animals did not survive the inoculation long enough for tuberculosis to develop.

HARBITZ, (9) examined at autopsy 142 cases of children & found that ofthe 91 cases in which there was neither macroscopic nor microscopic evidence of tuberculosis, 18 were tuberculosis on animal test. The material giving this result was in 13 instances the neck glands. In the other five cases the result was/

was produced by injection of the following:-

CASE 1. Tracheal gland.
" 2. Neck and mesenteric glands.
" 3. Mesenteric and retroperitoneal glands.
" 4. Neck, Tracheal and Mesenteric glands.
" 5. " and tracheal glands.

That latent tubercle bacilli may also be found in glands other than lymphatic glands has been pointed out by GOODALE (10) in his report on the clinical examination of children with enlarged tonsils He examined tonsils from 9 cases of children varying from 2 to 9 years old. The tonsils before being inoculated into guinea-pigs were examined histologically in 7 instances. Of the latter, 2 showed no tuberculous changes either to the macroscopic or microscopic examination yet they were instrumental in giving rise to a tuberculous infection in the experimented animals.

IPSEN (11) was able to demonstrate, during the course of his examination of 102 cases of children of which 74 were non-tuberculous, the presence of latent tubercle bacilli in the mesenteric glands of one case, aged 2 years. These glands on inoculation into guinea-pigs produced a tuberculous infection/

infection.

Again WEBER AND BAGINSKY (12) in their investigation have been able to establish the presence of latent tubercle bacilli in one case, that of a child of $2\frac{1}{2}$ years old, in a series of 26 children ranging from 3 months to $12\frac{1}{4}$ years of age. This case showed neither macroscopic nor microscopic evidence of tuberculosis, and the culture isolated from the cervical gland was of the bovine type.

BARTEL (13) has demonstrated that in 8 of 68 cases of children dying from measles, diphtheria or scarlet fever, in whom there was no macroscopic or microscopic tuberculous lesions, the glands (cervical, bronchial or mesenteric) were tuberculous on inoculation.

Other evidence has been furnished by the work of RABINOWITSCH (14). She mentions the case of a child, aged 14 months, who died of broncho-pneumonia, the cervical and mesenteric glands from which though normal in apperance in every respect, were able to produce tuberculosis in the inoculated animals.

Further instances of this latency are found in BEITZKE'S PAPER (15). He showed that among

27/

27 cases of children dying from diseases other than tuberculosis, 9 were tuberculous, the material employed for the test being the normal cervical, tracheobronchial and mesenteric glands.

Such examples of quiescent tubercle bacilli are not confined to the human body, for tubercle bacilli in a latent state have also been demonstrated in animals by RABINOWITSCH AND KEMPNER (16), and LINNENBRINK (17).

My study of 36 non-tuberculous cases (vide supra), in an attempt to elucidate the subject of latent tuberculosis, can be conveniently divided into 2 groups, one of adults and one of children. The adult group numbering 21 cases (one, case 39, being excluded as the inoculated animals died prematurely) is as follows:

(a) 7 cases in which the cervical, bronchial and mesenteric glands of each case were separately studied.

(b) 7 cases in which the mesenteric glands alone were studied.

(c) 3 cases in which the bronchial glands alone were investigated. (one case also includes the glands along the pancreas).

(d)/

(d) 1 case in which the cervical and bronchial glands were separately studied.

(e) 1 case in which the cervical and mesenteric glands were separately studied.

(f) 1 case of cervical glands.

(g) 1 case of retroperitoneal glands.

The other group that of children, consists of 14 cases as under: -

(a) 9 cases of mesenteric glands.

(b) 3 cases in which the cervical and mesenteric glands of each case were separately investigated.

(c) 1 case of the cervical, bronchial and mesenteric glands.

(d) 1 case of the bronchial glands alone.

The 21 adult cases, therefore, involve the separate study of the

Mesenteric glands 16 times.
Bronchial " 11 "
Cervical " 10 "

and in the 14 cases of children there was a separate study of the

Mesenteric glands 13 times.

Bronchial/

Bronchial glands 3 times.

Cervical " 4 "

As a result of animal inoculation three adults and one child yielded material which proved to be tuberculous. The microscopic examination of sections of the glands employed for the test gave negative results in 3 of these cases, while in the remaining case, that of an adult, tuberculous changes were found histologically. Hence 3 of my 34 cases (a second case has also been deducted by reason of its positive histological evidence of tuberculosis as just mentioned) were undoubted instances of latent tuberculosis, in which living tubercle bacilli were demonstrated in the tissues of the human body by means of animal inoculation, and yet in situ these produced no changes detectable by the microscope. These cases are:-

(a) The cervical gland in the case of a man aged 56 (case 25); the tubercle bacilli isolated were found to be of the human type.

(b) The bronchial and enlarged glands near the pancreas in the case of a woman, aged 61 (case 52). The culture raised was of low virulence for/

for the rabbit (human type).

(c) The mesenteric glands of a child aged 3 years and 6 months (Case 54). The culture obtained had the Cultural characters of the human tubercle bacilli and was found to possess a slight virulence for the rabbit.

Case 72. This is a case of a woman (referred to above) in whom, though no tuberculous changes were visible to the naked eye, yet a section of the retroperitoneal gland revealed histological evidence of the disease, and therefore strictly speaking, cannot be included as a case of latent tuberculosis.

Summarising the results obtained by various workers gives the following table: -

TABLE/

TABLE VIII.

AUTHORS.	NO. of CASES.	NO. of LATENT CASES.	PER-CENTAGE.	Glands in which latent tubercle bacilli were found.		
				CERVICAL.	BRONCHIAL.	MESENTERIC.
Kaeble.	23	2	8·7		2	
Harbitz.	91	18	19·7	16	3	3
Weber and Baginsky.	26	1	3·85	1		
Ipsen.	74	1	1·35			1
MacFadyean and MacConkey.	20	2	10·0			2
Bartel.	68	8	11·75	5(a)	3	2
Rosenberger.	21	6	28·5			
Goodall.	9	2	22·2	2(b)		
Own cases.	34	3	8·8	1	1(c)	1
	366	43	11·7	25	9	9

a= including 4 tonsils.
b= tonsils.
c= bronchial and retroperitoneal glands.

The evidence just stated points strongly to the occurrence of latent tuberculosis in man, but this view has met with opposition on the part of some investigators. Among those who do not share this view of latency, the foremost, perhaps, is JOEST (18) whose work I shall now attempt to discuss at some length partly, because of the extensive experiments he has performed on this subject and partly, on account of full data of his work being available.

In 1907 he published the results of his investigations concerning the question of the presence of latent tubercle bacilli in the lymphatic glands of spontaneously tuberculous cows and pigs. He inoculated these glands into guinea-pigs, while part of the glands was also submitted to an histological examination, but he failed to observe any tuberculous infection in the inoculated animals where the material used for the experiment was microscopically free from tuberculous changes. Such findings in numerous instances have led him to draw the Conclusion that latent tubercle bacilli in the lymphatic glands on the whole do not occur in the case of cows and/

and pigs.

In 1912 he recorded the results of his further research on this subject and not only did he then re-affirm his first contention, but also expressed the opinion that man, likewise, does not harbour latent tubercle bacilli. He employed for his investigation guinea-pigs divided into 3 sets, 9 in the first and 17 in each of the second and third sets. The animals belonging to the first two sets were each inoculated intramuscularly with a dose of ·000,005 grammes of human tubercle bacilli, while those in the third set were inoculated with the same quantity of tubercle bacilli of the bovine type in a like manner. They were killed at different stages, from 24 hours onwards, and the glands draining the areas of inoculation, in this case, the Inguinal and the Iliac glands were examined for any histological changes, and for the presence of tubercle bacilli. The results obtained by him were tabulated as under: -

SERIES.	1st appearance of tubercle bacilli after inoculation.	1st appearance of definite specific changes after inoculation.
I	2nd day	3rd day
II	1st "	3rd "
III	5th "	*6th "

From/

From this he infers that, if we were to understand by latent tubercle bacilli those which are found in a tissue without this tissue offering specific tuberculous changes, we should according to this definition, have to accept a latency of only one or two days. The short period between the first appearance of tubercle bacilli and that of specific tuberculous changes in the glands he interprets as an incubation stage, in that every infective agent cannot, at the moment when it lodges in a tissue, have generated specific histological lesions, and that these lesions can only be found after the expiration of a certain time (incubation period). During this interval the histological changes develop, till they have attained to such a degree that they can be clearly pointed out, and can then with certainty be called specific. He, therefore, asserts that the short time (1 to 2 days) which in his experiment lies between the first appearance of the tubercle bacilli in the lymphatic glands and the first specific changes is therefore to be considered as an incubation stage, and not as latency of tubercle bacilli in the tissue of the lymphatic glands.

The/

The conclusionshe draws are in direct contradiction to the results obtained by other investigatore and myself, and it is therefore necessary to try to find what cause or causes this apparent discrepancy is due to. In this connection, one or two fallacies which he committed in his deductions may be pointed out.

In speaking of latent tuberculosis, the following points must all be taken into consideration: -

1. The number of tubercle bacilli inoculated naturally and experimentally.
2. The virulence of the organisms at the time of inoculation.
3. The susceptibility, or the power of resistance of the body concerned.

1. One is inclined to assign an important influence to the quantity of tubercle bacilli in regard to the question of infection. It is not unreasonable to assume that latency of tubercle bacilli will more likely take place when minute doses of the infective organisms are inoculated; such is much more probable to occur in the natural than in the experimentally produced disease/

disease.

This objection JOEST tried to meet with the argument that in his experiment not only the Inguinal glands immediate to the site of inoculation were examined but also the Subiliac glands which, being situated further away from the source of infection, must necessarily, in his opinion, have received only a few tubercle bacilli, and yet they showed specific changes just as quickly as in the copiously infected Inguinal glands.

2. The virulence of the tubercle bacilli used must play an important part in the question of infection and, in this instance, particularly on the phenomena of latent tuberculous infection in that, tubercle bacilli of a certain virulence may rapidly cause specific changes in the lymphatic glands, such as happened in JOEST'S experiments; on the other hand, bacilli of less virulence (a thing not at all unlikely to occur under natural conditions) may lie inert in the body for a varying length of time (latent period) before reactive/

reactive lesions are developed. In this respect, JOEST'S experiments are far from being convincing in that, the tubercle bacilli employed by him belonged to a virulent strain.

3. Individual susceptibility. JOEST was, in all probability, in error in interpreting the results he obtained in guinea-pigs as applicable to man infected under natural conditions. Relying on this assumption, he denied, as mentioned, the possibility of tubercle bacilli lying latent in the human body. The power of resistance to tuberculous infection of animals, such as guinea-pigs, and that of man is widely different, at least in degree, if not in character. In the course of one's experiment one has found in a certain proportion of human cases, devoid of any signs of tuberculosis, glands, normal in appearance both macroscopically and microscopically, which nevertheless are capable of causing a tuberculous infection, in some instances even a generalised tuberculosis, in the guinea-pigs on inoculation. This, in itself, demonstrates that tubercle bacilli/

bacilli may lie inert in the glands of the human body under suitable conditions and yet be capable of bringing on an acute tuberculous infection when they are inoculated into a susceptible animal.

One may therefore, from the large amount of evidence accumulated, conclude, in spite of JOEST'S objections, that the existence of latent tuberculosis cannot be denied, and that it is to be found in a certain proportion of otherwise healthy individuals, probably an average of 10 per cent, as the appended table (VIII) shows, with perhaps variations at different periods of life. BARTEL and SPIELER (19) lay great stress on the importance of a lymphoid or pretubercular stage which is marked by a hyperplasia accompanied with swelling of the glands before there is any histological evidence of tuberculosis. How long tubercle bacilli may remain in the human body one cannot at present say with certainty from want of data. But in the case of animals BARTEL (20) has shown that tubercle bacilli may reside in the/

the tissue as long as 104 days without producing any characteristic changes. He used for his experiments rabbits and guinea-pigs which were fed with human tubercle bacilli, and found that the glands of the infected animals, though normal to histological and naked eye examination, contained tubercle bacilli, as were shown by their producing tuberculosis in animals on inoculation.

FREQUENCY/

FREQUENCY OF TUBERCULOUS INFECTION.

Much attention has of late been directed to the question of frequency of occurrence of tuberculosis in man, and a considerable amount of work bearing on this subject has been published and much of it has been widely accepted without comment. On account of the importance of this subject, it is necessary to review the more salient evidence that has been advanced in support of the contention that tuberculous infection is, at one time or another, to be found in nearly every individual.

The evidence which is available for the purpose of estimating the share taken by tuberculosis in the production of diseases in man, generally speaking, comes under three headings: -

1. Clinical evidence.
2. Experimental evidence based on the use of Tuberculin.
3. Post Mortem evidence.

1. Clinical evidence. In estimating the prevalence of the disease, any results based on this/

this evidence alone must necesarily be misleading, as it is universally recognised that in many cases of tuberculosis the lesions in the body may be and often are so minute as to escape the detection by the most elaborate clinical examination. This might lead to cases which are really tuberculous being overlooked. On the other hand, cases which are in fact something else may be wrongly diagnosed as tuberculosis., Besides personal bias is apt to have free play in this latter type of cases..

2. Cutaneous reaction. Many investigators in seeking to map out the extent of tuberculous infection in man have placed considerable reliance on this test either alone, or in combination with post mortem findings. VON PIRQUET (1) himself may be instanced as one who used this method. From the results of his tuberculin test he stated that beginning at birth tuberculosis is more frequent in succeeding years of life until at the period between 13 and 14 years of age

90/

90 per cent. or over of all individuals are affected and have tuberculous lesions somewhere in their body, either in an active or passive condition.

Figures comparable with these were similarly obtained by HAMBURGER and MONTI (2) who gave the following table: -

TABLE/

TABLE IX.

AGE IN YEARS.	NO. of CHILDREN EXAMINED.	NUMBER REACTED.	PERCENTAGE.
2	46	4	9
3	56	11	20
4	75	24	32
5	50	26	52
6	63	32	51
7	46	28	61
8	30	22	73
9	35	25	71
10	26	22	85
11	29	27	93
12	19	18	95
13	17	16	94
14	17	16	94
TOTAL	509	271	

Their observations, as such, have been confirmed elsewhere and in this country notably by McNEIL (3). It is not the intention of this work to discuss the value of this mode of examination or to measure to what extent it can solve this problem. Suffice it to mention the fact that in the applicability of the test in this direction support must be found in post mortem examination, and this it is necessary to discuss at some length.

3. Post Mortem evidence. It is mainly on the statistics obtained at autopsy by some continental observers that the opinion of the extraordinary wide-spread nature of this disease is based. In the well known paper published by NAEGELI (4) in 1900 on 500 cases observed at the post mortem rooms of the Zuricherishen pathologischen Institut, it was shown that, in 88 cases of children, 15 (18%) had lesions of tuberculosis; while in the case of adults, out of a total of 420 autopsies, 391 (93%) revealed evidence of/

of past or existing tuberculous lesions. Working on the same lines BURKHARDT (5) found that out of 190 children and 1262 adults, who had been examined post mortem, there were, respectively, 72 and 1149 cases showing lesions of tuberculosis, a percentage of 38 in the former case and 91 in the latter.

These authors regard as evidence of tuberculosis, besides obvious tuberculous changes, such lesions as calcareous or caseous glands or nodules. They even go so far as to include, without giving reasons for the procedure, all small fibrous nodules and scar tissue in the lungs among lesions of a tuberculous nature. This assumption, for such it is, characterises the works of many Continental writers on this subject. ALBRECHT and ARNSTEIN-WEIN (6) have conducted an investigation concerning the frequency of tuberculosis of the tracheo-bronchial lymphatic glands in 100 children between the age of 6 and 16 years. They found that/

that 38 of the 100 cases could, without hesitation, after a post mortem examination, be put down as cases of fatal or evidently advanced tuberculosis, and of the remaining 62 cases 36 were proved after a careful macroscopic examination to be positively tuberculous. There still remained, therefore, 26 cases of the 100 which even after the most careful naked eye examination did not show any signs of tuberculosis anywhere in the body, but by means, however, of histological examination of the glands, half of this number that is 13, were discovered to be tuberculous. Consequently, there remained in all only 13 cases as finally negative. Hence, in their opinion, among these 100 children there was a frequency of tuberculosis of about 87 per cent. But we find in their records of experiment that, among the 87 cases which they called tuberculous, 19 showed as the only lesion in the body some completely fibrous encapsulated calcareous nodules (Kalkherden) or hyaline nodules in the glands.

Besides/

Besides, there were 13 cases in their series diagnosed as tuberculous, the diagnosis being based on evidence furnished by histological examination only, but we are not told what was the nature of such histological evidence.

GHON (7) out of 644 post mortems conducted by himself at the St.Anne's Children's Hospital in Vienna found 184 tuberculous cases. Of these, we are told that in practically every instance a primary infection of the lung could be determined. The evidence for this statement was obtained by a "careful macroscopic" examination of the lungs and of the tracheo-bronchial glands. He states that, where these glands showed any tuberculous changes, he could almost invariably trace them to one or more primary foci in the lung which in some cases could be so small as not to exceed the size of a pin's head.

Among the cases which he regarded as tuberculous one finds the following examples: -

1. p.15. Sekt. Nr. 439 a male aged 6 years; a pea sized/

sized calcareous subpleural nodule at the apex of the left lower lobe, and caseation and induration of the tracheo-bronchial glands were discovered.

2. p.15. Sekt. Nr. 861. A male aged 8 years. A calcareous subpleural focus of pea size at middle of anterior surface of left lower lobe and calcification and contraction of the tracheo-bronchial glands.

3. p.16. Sekt. Nr. 850. A male aged $7\frac{1}{2}$ years. An ill-defined induration of bean size, with calcareous central nodule of pin head at right apex. Partial calcification and contraction of the glands.

4. p.16. Sekt. Nr. 742. A female aged 11 years. A greyish black induration of hemp seed size at right lower lobe with a pin head sized calcareous focus in a tracheo-bronchial gland.

5. p.37. Sekt. Nr. 642. a male aged $10\frac{1}{2}$ years. Three subpleural calcareous nodules of pea size at left lower lobe with partial calcification of the tracheo-bronchial glands.

6/

6. p.93. Sekt. Nr. 909. A male aged 5 years. A calcareous and contracted nodule of hemp seed size in upper apex of left lower lobe. Calcified and contracted tracheo-bronchial gland.

7. p.113. Sekt. Nr. 1001. A male aged 11½ years. A calcareous nodule of hemp seed size in left upper lobe. Small calcareous nodules in several tracheo-bronchial glands.

8. p.132. Sekt. Nr. 615. A female aged 14. A narrow scar in middle of upper right lobe, A calcareous nodule of poppy seed size in tracheo-bronchial gland.

Besides these, many other similar instances are found in the record of his cases. In none of the 8 cases quoted were there any lesions of tuberculosis elsewhere in the body and his diagnosis of the condition was founded purely on the macroscopic examination. Again he put on record (page 45) 5 more instances which presented on examination no other changes than a single scar in the lung, varying from the size of a hemp seed to that of a pea, and these/

these he regarded as tuberculous.

Sufficient has now been quoted to enable us to examine carefully into the whole subject. The assumption of the extreme frequency of tuberculosis, such as we are made to believe by NAEGELI and his followers, is mainly based on the fact that very often on the post mortem table in persons, who have died of diseases other than tuberculosis, tuberculous changes can be found. In many cases,however,only the most minute examination can reveal their presence. I shall now point out the more important fallacies associated with the work of those authors, who have asserted that tuberculosis is practically universal in human beings.

1. In the first place, the material with which NAEGELI and BURKHARDT have made their investigations is, with respect to age and source, quite inappropriate to allow a general conclusion to be drawn from it.

(a) It is inappropriate as regards age because it was derived from Infirmaries which are essentially frequented by people of adult age between 20 and 40, in whom

causes/

causes of death other than tuberculosis play a comparatively small part. The disease, on that account, comes moreinto the foreground than in a population normally composed of all ages.

(b) The material is further inappropriate with respect to its origin. The frequency of tuberculosis depends, to an important extent, on the social condition, since it is a fact that it occurs among the poor classes many times more often than among the better class. The Infirmaries, as charitable institutions, mostly accommodate patients belonging to the lower class and, therefore, the subjects which go to the post mortem room of these institutions, naturally in the majority of cases come under this categary. How can one then be allowed to draw from the findings, coming from such a source, a conclusion with respect to the total population ?

2. Besides, there is a further objection to the deduction of these observers. I do not doubt for/

for a moment that they have found, as often as they have stated, after a careful examination and after a long and searching pursuit, a very small nodule, scarcely as big as the head of a pin, in the lung or a slight pleuritic scar, or other small chalky deposits as calcareous nodules, either in the lung or in the bronchial glands. But I strongly contest their right to consider these lesions, without other substantiated evidence, as aetiologically equivalent to tuberculosis; for in their investigations a decisive factor has either been entirely overlooked or not recognised as an important element, namely the possibility, may be probability, of these lesions having resulted from causes other than tuberculosis. This consideration has led me to the investigation of cases in which on post mortem examination no evidence of tuberculosis was found other than some calcareous or caseous nodules in the lungs or glands.

The result I obtained (vide supra) is that such nodules from 5 out of 27 cases of adults gave rise to a tuberculous infection in guinea-pigs/

guinea-pigs on inoculation, an equivalent to 18·5%. In the cases of children 2 out of 8 were tuberculous with a similar test or equal to 25%. The Royal Commissioners (8) found that out of 7 cases 2, both being children, contained tubercle bacilli. EASTWOOD and GRIFFITH (9) have studied 16 similar cases in children and in 12 instances acid fast bacilli simulating tubercle bacilli could be demonstrated in smears, whereas none of them were found to infect guinea-pigs on inoculation. STANLEY GRIFFITH (10) has also investigated 5 cases in children of like nature. None of them, however, produced tuberculosis in guinea-pigs. Microscopic examination was positive in smears from one case out of three examined.

I have further investigated six consecutive cases in which no lesions of tuberculosis were found in any part of the body on gross examination (vide supra). As many of the bronchial glands as could be obtained were made into an Emulsion and injected into three guinea-pigs in each case. None of the animals developed tuberculosis/

tuberculosis. The lungs were then cut in thin slices and minutely examined for the presence of any nodules, either fibrous or calcareous in nature. In the three cases of children no such lesions were discovered. Among the three adult cases two showed the presence of these nodules. which, after preparation, were cut in serial sections, stained by ZIEHL-NIELSEN and examined for tubercle bacilli. In all, 1081 sections of these nodules were examined as carefully as possible but in none could tubercle bacilli be demonstrated, nor were histological changes resembling a definite tuberculous lesion found.

A Summary of the results of the cases investigated by different workers gives the following table.

TABLE/

TABLE X.

	TOTAL NO. of CASES.		ACID FAST BACILLI FOUND MICROSCOPICALLY.		TUBERCULOSIS PRODUCED in GUINEA-PIGS.		PERCENTAGE of TUBERCULOSIS.	
	ADULTS.	CHILDREN.	ADULTS.	CHILDREN.	ADULTS.	CHILDREN.	ADULTS.	CHILDREN.
ROYAL COMMISSION.	5	2	-	2	-	1	0	100
EASTWOOD & GRIFFITH.	-	16	-	12	-	-	-	75
STANLEY GRIFFITH.	-	5	-	1	-	-	-	20
OWN CASES.	27	8	Not undertaken.		5	2	18·5	25
" "								
FOR SERIAL SECTION.	2	-	-	-	Not undertaken.		0	0
	34	31		15	5	3	14·7	55 (a)

(a) If one only counts those in which tubercle bacilli were undoubtedly present as determined by animal inoculation, the percentage incidence of tuberculosis in these children cases is reduced to 9·7.

One/

One therefore finds that 14.7% of cases of adults gave a positive indication of tuberculosis on animal test; in children, if one were to include those cases in which acid fast bacilli morphologically identical to tubercle bacilli were demonstrated one gets a 55% of positive results, whereas if only those cases furnishing material which produced tuberculosis in guinea-pigs are taken into account, the percentage incidence is reduced to 9.7. Hence, there remains a large proportion of these cases, (not to speak of those presenting on examination no other changes beyond one or more scars in the lung,) which cannot be definitely accounted for, and yet these would be assumed by Naegeli and his followers to be of a tuberculous character. I do not deny, far from it, that some of these instances, (though neither the microscope nor animal inoculation could establish the presence of tuberculosis), may possibly or even probably be tuberculous at the start, but I certainly cannot accept the hypothesis as propagated by these authors who attribute every such case to a tuberculous origin.

In this connection, there is yet another important evidence which speaks against Naegeli's supposition. In dealing with the question of Latent Tuberculosis/

Tuberculosis, (vide supra), I have shown that only in about 10 per cent of cases where no tuberculous lesions were demonstrated, macroscopically or microscopically, were latent tubercle bacilli proved to be present on animal inoculation. The tissues employed for this test were the tonsils, the cervical, the bronchial and the mesenteric glands. If Naegeli and his supporters were right in their hypothesis one would have expected that these glands draining, as they do, the important channels, whereby tuberculous infection is conveyed to the body, should reveal lesions of tuberculosis in a large proportion of cases, and should generally, though not invariably, be capable of carrying infection to the inoculated animals.

Without the slightest intention of disregarding the great prevalence of the disease, I conclude, on the ground of the arguments already outlined, that, unless convincing evidence is forthcoming in the future, it is rash and unwarrantable at the present time to put reliance on the view of Naegeli and his pupils, that tuberculosis is really a disease so universal as to be found in nearly all persons at one time or another of their existence.

INCIDENCE OF "BOVINE" INFECTION.

KOCH'S contention that bovine tuberculosis was not communicable to man to any material extent has been definitely refuted by a host of observers, among whom in this country may be mentioned The ROYAL COMMISSIONERS, DELÉPINE, FRASER, and MITCHELL. It is, therefore, unnecessary to enlarge on this subject, beyond tabulating the results obtained by different investigators and myself. It is noteworthy to record that, as early as 1891, DELÉPINE (1) had pointed out the dangers of infection through the alimentary canal associated with the consumption of contaminated milk, and in 1901 definitely proved by the result of his experiments on 4 calves that tubercle bacilli from mixed tuberculous sputa of human subjects were infectious to cattle.

As elsewhere stated, in the investigation of my cases care has been taken to avoid, as far as possible, any element of selection, that is, all material obtained from the different sources was examined regardless of the history of the case previous/

previous to post mortem.

The cases appended here are tabulated according to the rules laid down by PARK and KRUMWIEDE (2) who recommend their adoption in classifying each individual case with the view to secure tabulations of cases which are comparable.

1. "Pulmonary tuberculosis: - Where the lesions are confined to the thoracic organs, clinical or post mortem diagnosis. A few lesions elsewhere disregarded, especially where abdominal lesions were present which might be regarded as infection by ingestion rather than true generalisation".
2. "Tuberculous adenitis: - Other than cervical or internal nodes".
3. "Tuberculous adenitis: - Cervical. Where the nodes are apparently only infected or this lesion is overwhelmingly predominant. Where this lesion is primary as far as could be ascertained. If abdominal lesion also, is classified under that heading. If part of a generalised tuberculosis is classified under that/

that heading".

4. "Abdominal Tuberculosis: - Tuberculosis of intestines, abdominal lymph nodes or peritoneum, with or without tubercles in the spleen or liver. They may be coincident lesions in the Cervical nodes. If there was spreading to thoracic organs see generalised tuberculosis".
5. "Generalised Tuberculosis".
6. "Tubercular meningitis: - Clinical diagnosis, extent of generalisation unknown, or associated with localised lesions elsewhere".
7. "Tuberculosis of bones and joints: - Where these lesions are the essential part of the disease".
8. "Tuberculosis of the genito-urinary organs".
9. "Tuberculosis of skin".
10. "Miscellaneous cases".

TABLE/

TABLE XI.

OWN CASES.

CLASSIFICATION.	ADULTS AND 16 YEARS OVER.		CHILDREN 5-16 YEARS.		CHILDREN UNDER 5 YEARS.	
	HUMAN.	BOVINE.	HUMAN.	BOVINE.	HUMAN.	BOVINE.
PULMONARY TUB.	12	-	1	-	1	-
SPUTUM.	28	1	-	-	-	-
ABDOMINAL TUB.	2	2	1	1	-	2
GENERALISED TUB.	5	2	1	2	1	1
TUB. MENINGITIS.	5	-	-	3	2	-
DIS. GENITO-URINARY.	1	-	-	-	-	-
DISEASE of SKIN.	2	-	-	-	-	-
TUB. ADEN. CERVICAL.	1	-	-	-	-	-
TUB. BONES & JOINTS.	-	-	-	-	1	-
MISCELLANEOUS:						
LATENT TUB.	2	(a)1	-	-	1	-
CALC. or CASEOUS TUB.	3	1	-	-	-	2
	61	7	3	6	6	5

TOTAL 88.

(a) Case 72; microscopic examination of section positive.

Expressing these cases in percentages of bovine infection gives the following table: -,

TABLE. XII.

OWN CASES in PERCENTAGE INCIDENCE of BOVINE INFECTION.

CLASSIFICATION.	ADULTS 16 YEARS AND OVER.	CHILDREN 5–16 YEARS.	CHILDREB UNDER 5 YEARS.
PULMONARY TUB.	0%	0%	0%
SPUTUM.	3·45%	–	–
ABDOMINAL TUB.	50·00%	50·00%	100·00%
GENERAL. TUB.	28·57%	66·66%	50·00%
TUB. MENINGITIS.	0%	100·00%	0%
DIS. GENITO-URINARY.	0%	–	–
DISEASE of SKIN.	0%	–	–
TUB. ADEN. CERVICAL.	0%	–	–
TUB. BONES & JOINTS.	–	–	0%
MISCELLANEOUS:			
LATENT TUB.	(a)33·30%	–	0%
CALC. or CASEOUS TUB.	25·00%	–	100·00%
PERCENTAGE to TOTAL CASES in EACH GROUP.	10·29%	66·66%	45·45%

(a) Case 72. refer previous table.

TABLE/

TABLE XIII.

Tabulation according to seat of primary infection of 59 cases, other than sputum, including 39 adults and 20 children.

SEAT of ENTRY.	No. of CASES.	PERCENTAGE.
RESPIRATORY.	22	37·3
ALIMENTARY		
tonsils & cervical	3	5·1
intestine.	18	30·5
EVIDENCE INCONCLUSIVE.	16	27·1
	59	100·0.

TABLE showing relation of bovine infection to portal of entry.

TABLE XIV.

I. Adult cases, other than Sputum, (over 16 years).

PORTAL of ENTRY.	No. of CASES.	PERCENTAGE to TOTAL CASES.	BOVINE CASES.	PERCENTAGE of BOVINE INFECTION.
RESPIRATORY.	20	51·30	0	0
ALIMENTARY				
tonsil & cervical.	1	2·57	0	0
intestine.	8	20·50	5	62·5
EVIDENCE INCONCLUSIVE.	10	25·63	1	10·0
	39	100·00	6	15·4

II. Children Cases, other than sputum (under 16 years).

PORTAL of ENTRY.	No. of CASES.	PERCENTAGE to TOTAL CASES.	BOVINE CASES.	PERCENTAGE of BOVINE INFECTION.
RESPIRATORY.	2	10·0	0	0
ALIMENTARY.				
tonsil & cervical.	2	10·0	0	0
intestine.	10	50·0	9	90
EVIDENCE INCONCLUSIVE.	6	30·0	2	33
	20	100·0	11	55

FRASER (3) has investigated 70 cases of tuberculosis of bones and joints, MITCHELL (4) 72 cases of tuberculosis of the cervical glands, and GRIFFITH (5) 43 sputum cases. If we combine their results with my own, and further note that the material furnishing these investigations was all obtained in Edinburgh, the following table is formed, representing what one might call the Edinburgh statistics.

TABLE/

TABLE. XV.

EDINBURGH STATISTICS.

CLASSIFICATION.	ADULTS 16 YEARS AND OVER.		CHILDREN 5-16 YEARS.		CHILDREN UNDER 5 YEARS.	
	HUMAN.	BOVINE.	HUMAN.	BOVINE.	HUMAN.	BOVINE.
PULMONARY TUB.	12	-	1	-	1	-
SPUTUM CASES.	70	2	-	-	-	-
ABDOMINAL TUB.	2	2	1	1	-	2
GENERAL. TUB.	5	2	1	2	1	1
TUB. MENINGITIS.	5	-	-	3	2	-
DIS. GENITO-URINARY.	1	-	-	-	-	-
DISEASE of SKIN.	2	-	-	-	-	-
TUB. ADEN. CERVICAL.	1	-	4	26	3	39
TUB. BONE & JOINT.	3	-	11	9	13	(a)35
MISCELLANEOUS:						
LATENT TUB.	2	(b)1	-	-	1	-
CALC. or CASEOUS TUB.	3	1	-	-	-	2
	106	8	18	41	21	79

TOTAL 273

(a) including 3 mixed strains.

(b) case 72. refer above.

Expressing these cases in percentages of bovine infection gives the following table: -

TABLE. XVI.

EDINBURGH STATISTICS.

INCIDENCE of BOVINE INFECTION.

CLASSIFICATION.	ADULTS 16 YEARS AND OVER.	CHILDREN 5-16 YEARS.	CHILDREN UNDER 5 YEARS.
PULMONARY TUB.	0%	0%	0%
SPUTUM.	2·8%	–	–
ABDOMINAL TUB.	50·0%	50·0%	100%
GENERAL. TUB.	28·8%	66·6%	50·0%
TUB. MENINGITIS.	0%	100%	0%
DIS. GENITO-URINARY.	0%	–	–
DISEASE of SKIN.	0%	–	–
TUB. ADEN.CERVICAL.	0%	86·6%	92·9%
TUB. BONE & JOINT.	0%	45·0%	(a)73·0%
MISCELLANEOUS:			
LATENT TUB.	(a)33·3%	–	0%
CALC. or CASEOUS TUB.	25·0%	–	100%
PERCENTAGE of BOVINE INFECTION to TOTAL CASES in EACH GROUP.	7·02%	69·5%	79·0%

(a) refer previous tables.

It/

It is evident when we compare these data with those given below (Tables XVII - XX) that in Edinburgh the incidence of bovine infection, based on the results of 273 cases investigated by FRASER, MITCHELL, GRIFFITH and myself, is much higher than elsewhere, but in comparing these statistics with those of any other locality, the local conditions of the place must, at the same time, be taken into consideration.

For the purpose of providing comparison, the following table is prepared of all cases investigated in this country, with the exclusion of those of Edinburgh. It embodies 127 cases of the ROYAL COMMISSION (6) (included in these are also 20 cases of lupus)*, 78 children cases of EASTWOOD and GRIFFITH (7), 35 children cases of STANLEY GRIFFITH (8), 23 Sputum cases of BULLOCH (9) and 105 Sputum cases also of STANLEY GRIFFITH (5). The recent work of EASTWOOD and GRIFFITH (10) (11), is also included comprising 261 Bone and Joint cases, and 17 cases of diseases of the genito-urinary tract, making a total of 646 cases.

TABLE/

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* One of their cases, H.34, is omitted as the age is not given.

TABLE. XVII.

STATISTICS of GREAT BRITAIN, excluding EDINBURGH.

CLASSIFICATION.	ADULTS 16 YEARS AND OVER.		CHILDREN 5-16 YEARS.		CHILDREN UNDER 5 YEARS.	
	HUMAN.	BOVINE.	HUMAN.	BOVINE.	HUMAN.	BOVINE.
PULMONARY TUB.	13	-	13	-	10	-
SPUTUM.	154	2	-	-	-	-
ABDOMINAL TUB.	-	(a)2	3	4	14	16
GENERAL. TUB.	-	-	16	-	14	(b)4
TUB. MENINGITIS.	-	-	12	2	28	(b)7
DIS. GENITO-URINARY.	15	3	2	-	-	-
DISEASE of SKIN.	7	3	3	6	1	-
TUB. ADEN. CERVICAL.	-	-	5	2	1	1
TUB. BONE & JOINT.	(c)48	4	(d)137	38	(e)34	14
MISCELLANEOUS:						
LATENT TUB.	-	-	2	2	2	1
OTHER TUB.	-	1	-	-	-	-
	237	15	193	54	104	43

TOTAL 646.

(a) including 1 intermediate strain.
(b) " 1 mixed "
(c) " 3 atypical strains.
(d) " 5 " "
(e) " 2 " "

The following table is obtained when these cases are expressed in percentage incidence of bovine infection.

TABLE./

TABLE. XVIII.

INCIDENCE of BOVINE INFECTION in GREAT BRITAIN, excluding EDINBURGH.

CLASSIFICATION.	ADULTS 16 YEARS AND OVER.	CHILDREN 5-16 YEARS.	CHILDREN UNDER. 5 YEARS.
PULMONARY TUB.	0%	0%	0%
SPUTUM.	1·3%	–	–
ABDOMINAL TUB.	(a)100·0%	57·0%	53·0%
GENERAL. TUB.	–	0%	22·2%
TUB. MENINGITIS.	–	14·3%	20·0%
DIS. GENITO-URINARY.	16·6%	0%	–
DISEASE of SKIN.	30·0%	66·6%	0%
TUB. ADEN. CERVICAL	–	28·5%	50·0%
TUB. BONE & JOINT.	7·7%	21·7%	29·2%
MISCELLANEOUS:			
LATENT TUB.	–	50·0%	33·3%
OTHER TUB.	(b)100%	–	–
PERCENTAGE to TOTAL CASES in EACH GROUP.	5·95%	21·9%	29·2%

(a) based on two cases.
(b) " " one case.

The/

The following is a complete table of all cases reported up to the present time. It comprises the

1,511 cases collected by PARK and KRUMWIEDE (12) which include those of the BRITISH ROYAL COMMISSION (6) and BULLOCH (9)

356 " of EASTWOOD and F.GRIFFITH (7), (10) and (11),

183 " of STANLEY GRIFFITH (5), and (8),

70 " of FRASER (3),

72 " of MITCHELL (4), and

88 " of my own.

Making a grand total of 2,280 cases.

TABLE/

TABLE XIX.

COMBINED TABLE of ALL CASES.

CLASSIFICATION.	ADULTS 16 YEARS AND OVER.		CHILDREN 5-16 YEARS.		CHILDREN UNDER 5 YEARS.	
	HUMAN.	BOVINE	HUMAN.	BOVINE.	HUMAN.	BOVINE.
PULMONARY TUB. including SPUTUM.	965	5	28	–	45	1
ABDOMINAL TUB.	18	(a)6	10	13	29	34
GENERAL. TUB.	45	3	35	7	169	(b)22
TUB. MENINGITIS.	6	–	13	5	55	(b)10
DIS. GENITO-URINARY.	35	4	4	–	–	–
DISEASE of SKIN.	12	3	4	6	2	–
TUB. ADEN. CERVICAL.	37	1	41	48	18	63
" " AXILLARY.	3	–	4	–	2	–
TUB. BONE & JOINT.	(c)76	4	(d)184	50	(e)73	(f)49
MISCELLANEOUS:						
LATENT TUB.	2	1	2	2	4	1
CALC. or CASEOUS TUB.	3	1	–	–	–	2
OTHER FORMS.	2	1	–	1	–	–
	1,204	29	325	132	397	182

TOTAL 2,269.

Mixed strains reported by PARK and KRUMWIEDE – 11 TOTAL 2,280.

(a) including 1 intermediate strain.
(b) " 1 mixed "
(c) " 3 atypical strains.
(d) including 5 atypical strains.
(e) " 2 " "
(f) " 3 mixed "

Expressing these cases in Percentage Incidence gives the following table.

TABLE/

TABLE. XX.

CLASSIFICATION.	ADULTS 16 YEARS AND OVER.	CHILDREN 5-16 YEARS.	CHILDREN UNDER 5 YEARS.
PULMONARY TUB.	0·51%	0%	2·17%
including SPUTUM.	25·00%	56·50%	61·30%
ABDOMINAL TUB.	6·25%	16·70%	16·60%
GENERAL. TUB.	0%	27·70%	15·40%
TUB. MENINGITIS.	10·26%	0%	–
DIS. GENITO-URINARY.	20·00%	60·00%	0%
DISEASE of SKIN.	2·63%	53·90%	77·70%
TUB. ADEN. CERVICAL.	0%	0%	0%
" " AXILLARY.	5·00%	21·40%	40·20%
TUB. BONE & JOINT.			
MISCELLANEOUS:			
LATENT TUB.	33·30%	50·00%	20·00%
CALC. or CASEOUS TUB.	25·00%	–	100·00%
OTHER FORMS.	33·30%	100·00%	–
PERCENTAGE INCIDENCE to TOTAL CASES in EACH GROUP.	2·35%	28·90%	31·43%

SUMMARY/

SUMMARY.

I. Incidence of Bovine Tuberculous Infection.

1. Cultures consisting of 125 strains from 88 cases of tuberculosis in man have been investigated. The material furnishing the cultures was obtained from

a. 14 cases of pulmonary tuberculosis.
b. 29 " " sputum.
c. 8 " " abdominal tuberculosis.
d. 12 " " generalised tuberculosis.
e. 10 " " tuberculous meningitis.
f. 2 " " lupus.
g. 1 " " tuberculosis of the genito-urinary tract.
h. 1 " " tuberculous cervical adenitis.
i. 1 " " tuberculosis of bone and joint.
j. 4 " " latent tuberculosis.
k. 6 " " calcareous or caseous tuberculosis.

2/

2. The strains isolated from these cases fall readily into one or other of the two groups, that is, either "Human" or "Bovine" type of tubercle bacillus; in no instance was an atypical strain demonstrated.

3. When two or more strains were isolated from a single case, their growth was identical in cultural characters and they were of the same virulence for the rabbit, that is, no mixed strains of tubercle bacilli were met with, consisting of a mixture of the human and bovine type.

4. In the sixty-eight cases of adults, bovine tubercle bacilli were isolated in seven instances.

   a.* 1 of 29 cases of sputum.

   b. 2 of 4 " " abdominal tuberculosis.

   c. 2 of 7 " " generalised tuberculosis.

   d. 1 of 22 " " in which there was no macroscopic evidence of tuberculosis.

   e. 1 of 27 " in which the only lesions were calcareous or caseous nodules.

5. Of 8 cases showing primary lesions in the intestines five were infected with tubercle bacilli

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* (It is to be specially noted that only 3 other cases of bovine tubercle bacilli in pure state being isolated from the sputum have been recorded.)

bacilli of the bovine type = 62·5%.

6. Of the twenty cases of children under 16 years of age bovine tubercle bacilli were isolated in eleven instances.

   a. 3 of 4 cases of abdominal tuberculosis.

   b. 3 of 5 " " generalised tuberculosis.

   c. 3 of 5 " " tuberculous meningitis.

   d. 2 of 8 " in which the only lesions were calcareous or caseous nodules.

7. Of 10 cases showing primary lesions in the intestine 9 were found infected with tubercle bacilli of the bovine type = 90%.

II. Cases in which the only lesions simulating tuberculosis found were of the character of either calcareous or caseous nodules.

1. Twenty seven cases of adults belonging to this group have been studied, and five were found tuberculous. Cultures raised from four were isolated and they furnished three human and one bovine strain.

2. Eight cases of children have been investigated and two were found tuberculous, both furnishing cultures of the bovine type.

III. Latent Tuberculosis.

1. Twenty-one cases of adults in which there was neither macroscopic nor microscopic evidence of tuberculosis have been investigated; cultures were isolated from two of them, both belonging to the human strain.

A culture belonging to the bovine type of tubercle bacillus was also obtained from another case of this group. In this case a microscopic examination of a section of the gland employed for inoculation revealed evidence of tuberculosis, this was undetected by the naked eye.

2. From one of fourteen cases of children of this group, a culture belonging to the human type of tubercle bacillus was isolated.

IV. General.

1. Differentiation between the human and bovine tubercle/

tubercle bacillus by the microscopic examination alone is unreliable.

2. Cultural characters, as a means of distinguishing the two types of tubercle bacillus can be depended upon, except in a small minority of cases when a mixed or an atypical strain of culture is present.
3. The most certain and at the same time most economical way of differentiating these two types is by means of inoculation into the rabbit.
4. Von Behring's theory of infection of the lung by way of the intestinal tract does not hold true for an overwhelming majority of cases.
5. Latent tuberculosis in man is proved to exist and is present in about 10 per cent of otherwise non-tuberculous subjects.
6. The incidence of tuberculous infection in adults alleged by some writers to be over 90 per cent is exaggerated and based on doubtful and unconvincing evidence.

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ACKNOWLEDGMENTS.

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Last/

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SUBJECTS of DISCUSSION

in the Text.

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